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Systematic Review on Thiazole Compounds as Nanoparticles: Chemistry, Synthesis, Antimicrobial Activities, Therapeutic Investigation

Soliman Soliman[1], Ali Soliman[1], Khalid Alzoubar[2], Joumaa Merza[1], and Ali Alasmi[1]

[1]*Department of Chemistry,*
Faculty of Sciences,
Al-Baath University,
Homs, Syria
[2]*Department of Chemistry,*
Faculty of Sciences,
Al-Furat University,
Deir Ez-Zor, Syria

1.3-thiazole is a unique heterocycle containing nitrogen and sulphur atoms. Thiazole chemistry has developed after the pioneering it of Hofmann and Hantzsch in 1887. Thiazole occupies an important place in medicinal chemistry. It is widely found in diverse pharmacologically active substances and in some naturally occurring compounds. In last decade, heterocyclic compounds containing thiazole moiety and their derivatives were found exhibiting nanoscale properties. In addition, they exhibit a wide spectrum of biological activities such as antioxidant, antitubercular, anti-inflammatory, anti-HIV, antitumor, anticonvulsive, antifungal and antibacterial. Thiazole is an essential in many natural (vitamin B_1—thiamine) and synthetic medicinally important compounds. This review focus on both the chemical and biological importance of thiazole as a nanoparticle and the different methods of synthesis of substituted thiazole with potential activities, which are now in developing phase.

1.3-тіазол є унікальним гетероциклом, що містить атоми Нітроґену та Сульфуру. Тіазолева хемія розвинулася після започаткування неї Гофманном і Ганчшем у 1887 році. Тіазол займає важливе місце в лікарській хемії. Він широко зустрічається в різних фармакологічно активних речовинах і в деяких природніх сполуках. В останнє десятиліття було виявлено, що гетероциклічні сполуки, які містять тіазолову частину, та їхні похідні проявляють нанорозмірні властивості. Крім того, вони проявляють широкий спектер біологічних дій, таких як антиоксидант-

на, протитуберкульозна, протизапальна, анти-ВІЛ, протипухлинна, протисудомна, протигрибкова та антибактеріяльна. Тіазол є незамінним у багатьох природніх (вітамін B_1 — тіамін) і синтетичних лікувально важливих сполуках. Цей огляд зосереджений як на хемічному, так і на біологічному значенні тіазолу як наночастинки, а також на різних методах синтези заміщеного тіазолу з потенційною активністю, які зараз знаходяться на стадії розробки.

Key words: thiazole, synthesis, anticonvulsant, antifungal, anti-HIV pharmacologically active nanoparticles.

Ключові слова: тіазол, синтеза, протисудомні, протигрибкові, анти-ВІЛ фармакологічно активні наночастинки.

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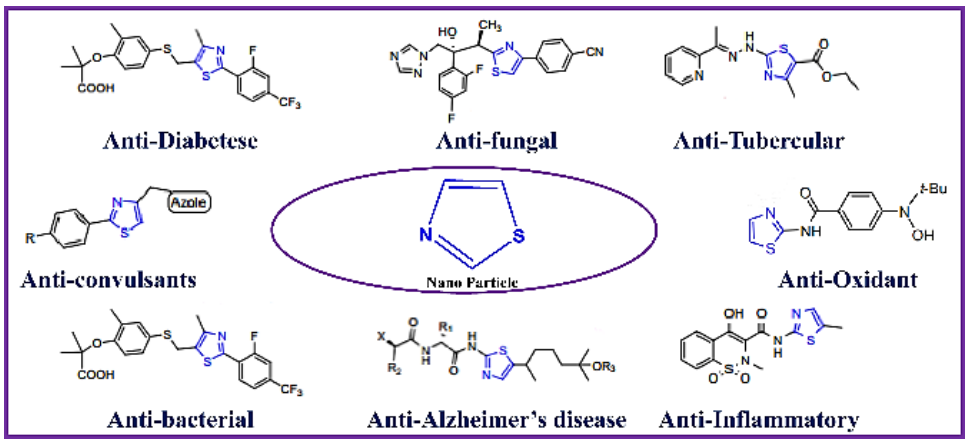
1. INTRODUCTION

A heterocyclic compound is one that possesses a cyclic structure with at least two different kinds of heteroatoms in the ring [1, 2], considered to be aromatic as it follows the Hückel's rule [3].

Thiazoles are an important class of heterocyclic compounds, found in many potent biologically active molecules such as fentiazac and meloxicam (both anti-inflammatory agents), nizatidine (antiulcerative agent), and sulphathiazole (antibacterial agent). Thiazoles are also frequently a vital component of novel and structurally diverse natural products that exhibit a wide variety of biological activities [4].



Heterocyclic compounds are attractive to medicinal chemists because of their unique chemical properties and wide-field biological activities. Sulphur is capable of forming both σ and π bonds; there-

fore, the studies of their binding interaction with receptor moiety was also an interesting field of research during last few years [5]. As one of basic five-membered heterocycles, the thiazole substructure is widely found in many bioactive natural products including the cytology compound thiazole [6–9]. On the other hand, the thiazole ring is present in various marine or terrestrial natural compounds that have useful biological activities [10–13]. In the recent years, experimental researches have introduced some thiazole derivatives as the multitherapeutic effect compounds including anticancer, anti-inflammatory, and inhibitor of the parasites like *Leishmania* and the fungi such as *Candida* [14–17].

The pattern of thiazole ring was carefully selected to confer different electronic environment to the molecules [18] therefor, consider it is a principal material for various chemical compounds including sulphur drugs, biocides, fungicides, dyes, and chemical reaction accelerators [18]. In addition, thiazole derivatives are reported to exhibit significant biological activities and are widely used as pharmaceuticals. Finally, careful science survey that thiazole ring systems have occupied a unique position in the design and synthesis of novel biological active agents with remarkable analgesic activities [19–22].

Nanotechnology takes us to the comprehensiveness of things represented in the study of the applications of very small things (nanomaterials) that can be used in a wide variety of fields from science, engineering and even life sciences. From this standpoint, we find that nanomaterials are the cornerstone and the first and basic building block in nanoscience and nanotechnology. One of the applications of nanomaterials is to increase the efficiency of electronic devices and at the same time reduce their size and reduce the energy consumed to operate these devices. This is evident in mobile devices, computers and data storage chips. Develop and improve the world of food, from the cultivation of grain to its packaging, in addition to working to increase the quality of food, maximizing its usefulness and maintaining its safety. Work to transfer the drug directly to the diseased cells.

2. THIAZOLE CHEMISTRY

Although the history of thiazole dates from 1879 with the work of Hofmann on benzothiazoles, the systematic study of parent heterocycle and its derivatives was reported from Hantzsch laboratory in 1887 [23]. Since then, a vast amount of work in the field of thiazole chemistry has been reported in the literature covering different aspects such as methods of synthesis, physical properties, structure and reactivity, reaction mechanism, industrial and biological appli-

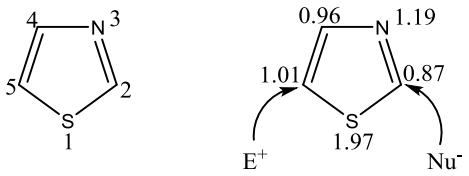


Fig. 1. Nomenclature and electronic structure of thiazole.

Fig. 2. The molecular geometry and charge distribution figures.

cations. Excellent books on thiazole containing up to date information on the subject have appeared [24]. It was necessary to give it a gist of modem concepts of structure and reactivity of thiazoles as a background.

Thiazole is an important aromatic containing sulphur and nitrogen atoms as a part of five-membered heterocyclic ring with the molecular formula of C_3H_3NS and molecular weight of 85.128 $g \cdot mole^{-1}$ (Figs. 1, 2). That thiazole is yellow in colour and is liquid in state. It is completely soluble in water at room temperature and miscible with most of the organic solvents, boiling point of 117–118°C having dipole moment 1.6*D* [25, 26]. Thiazole was characterized by larger π-electron delocalization and has therefore greater aromaticity. This is evidenced by the position of the ring protons in NMR (between δ, ppm 7.40 and 8.88 ppm) clearly indicating a strong diamagnetic ring current, and its Fourier infrared (IR) spectrum recorded in the 400–4000 cm^{-1} wavenumber region with a nine fundamental bands are analysed. The calculated π-density marks C5 as the primary electrophilic site and C2 as the nucleophilic site [27].

Thiazole is aromatic on the basis of delocalization of a lone pair of electrons from the sulphur atom completing the needed 6 π-electrons to satisfy Hückel's rule [23]. The resonance forms are presented in Fig. 3.

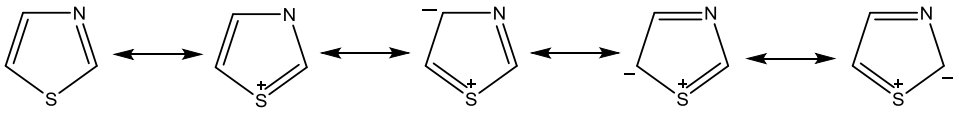


Fig. 3. The resonance forms of thiazole.

A lot of works has been done in the last few decades on the thiazole ring. Additionally, according to various studies conducted on thiazole and its derivatives, some of the compounds reportedly can be used to make polymers, liquid crystals, fluorescent dyes, herbicides, and insecticides [28].

2.1. Spectral Data of Thiazole [29–33]

UV (CH_3OH): λ_{max} 235 nm due to $\pi \rightarrow \pi^*$ transitions, 210 nm due to $\pi \rightarrow \pi^*$ transitions.

IR (KBr): 3140, 1500, 1360, 1250, 740 cm^{-1} absorptions.

^{1}H-NMR(DMSO-d6): δ 8.8(C–H), 7.4(C–H) and 7.9(C–H).

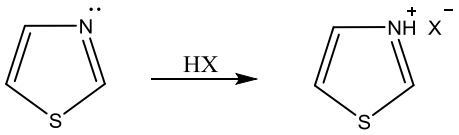
^{13}C-NMR (DMSO-d6): δ 153.6(C_2–H), 119.6(C_4–H), and 143.3(C_5–H).

Mass: *m/z* (relative intensity) 102(8), 101(25), 100(100), 74(3), 73(18), 60(7), 59(4), 58(75), 57(10), 55, 46, 45, 44, 42, 41, 40, 29, 27.

3. SUBSTITUTION REACTIONS OF THIAZOLE

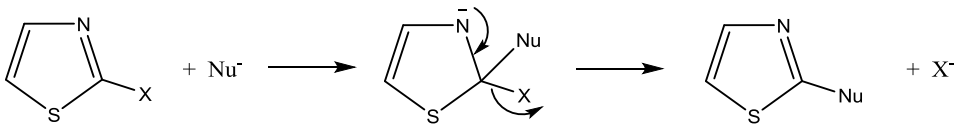
3.1. Nucleophilic Substitution

Conventional structure (I) having a lone pair of electrons on nitrogen explains the electrophilic attack of proton acids and alkyl halides to form thiazolium salts [34, 35]:



(I)

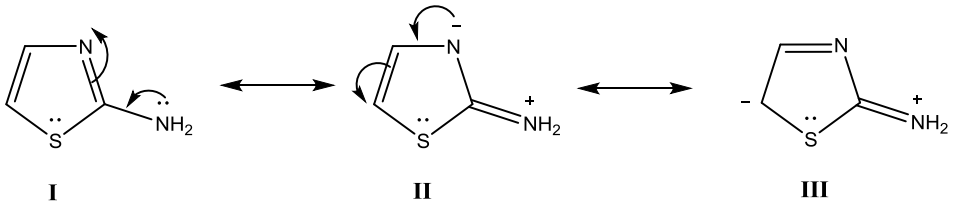
Canonical form (I) accounts for the reactivity of a proton or an appropriate group towards nucleophilic attack at position 2. The reactivity of 2-halogenothiazoles by nucleophilic reagents according to S_NAr mechanism is noteworthy [36, 37]:



3.2. Electrophilic Substitution

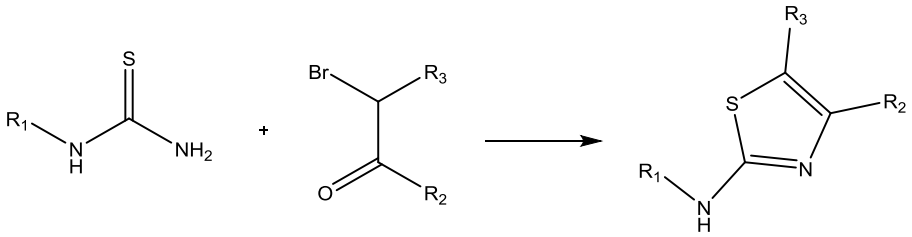
Canonical structure (III) of 2-substituted thiazole through the tran-

sient form (II) is facilitated when delocalisation of 7t-electrons of (I) from electron donating group at 2-position to 5-position via ring nitrogen takes place according to the principle of vinylogy [38–40]. The presence of a strong electron-donating group (like NH_2, OH, SH) or their alkyl or acyl derivative promotes delocalization to a great extent as illustrated by the following structures:

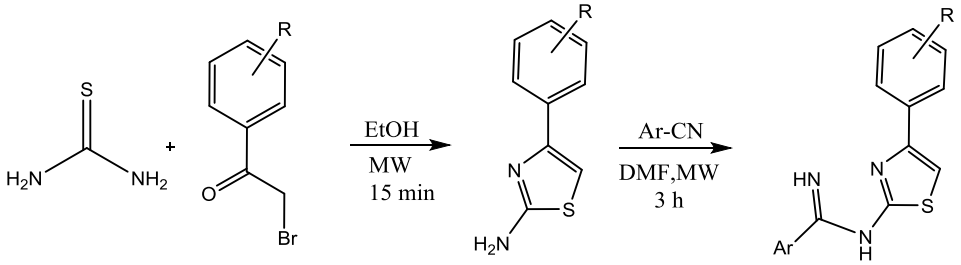


4. SYNTHESIS OF THIAZOLE AND ITS DERIVATIVES

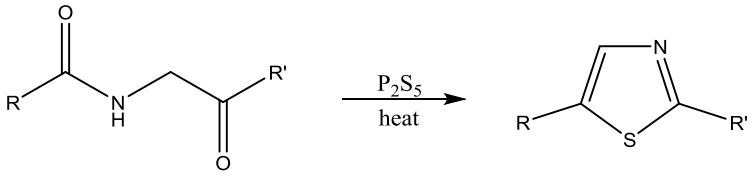
Canonical various synthetic methods exist for the construction of thiazole ring. The most common and oldest one is Hantzsch thiazole synthesis that is a reaction between α-haloketones and thioamides. 2-Aminothiazoles can be synthesized cleanly and in high yields via the Hantzsch thiazole synthesis. The large number of commercially available α- bromoketones makes this an attractive way to introduce diversity at the R2 and R3 positions of the thiazole ring [41]:



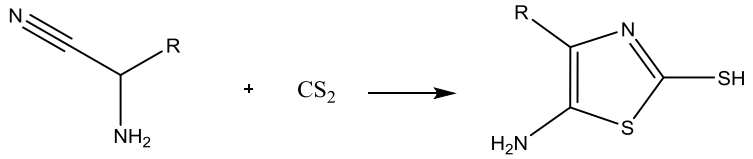
For example, Deau *et al.* reported microwave-assisted synthesis of novel N-(4-phenylthiazol-2-yl)-carboximidamides. The required intermediates 2 namely 4-phenylthiazol-2-amines were prepared by irradiating a mixture of thiourea and substituted α-bromoacetophenone, in ethanol for 15 min in excellent yields [42]:



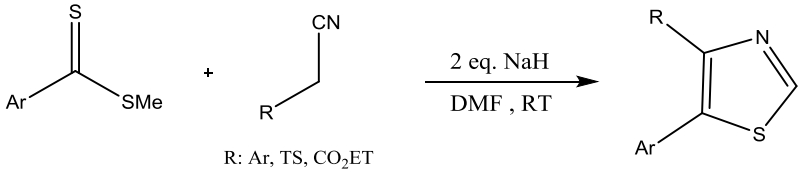
Gabriel's synthesis is another example of thiazole ring closure reaction of an acylamino-ketone with phosphorus pent sulphide yields the corresponding 2,5-disubstituted thiazole [43]:



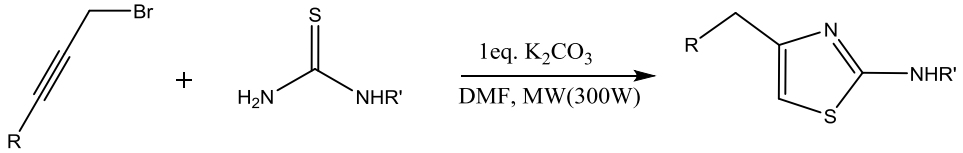
The Cook–Heilbron thiazole synthesis describes the reaction of α-aminonitriles with carbon disulphide to form 5-amino-2-mercaptothiazoles [44]:



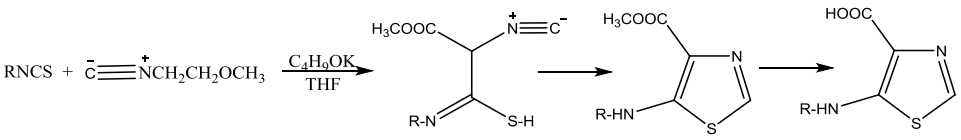
The reaction of isocyanides containing active-methylene with methyl carbodithioates in the presence of NaH as a base affords 4,5-disubstituted thiazoles (this method is simple, rapid, and efficient [45]):



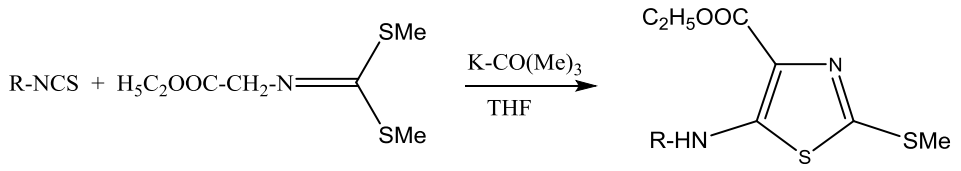
A domino alkylation-cyclization reaction of propargylic bromide derivatives with thioureas yields 2-aminothiazoles. This domino reaction was performed under microwave irradiation and in the presence of K_2CO_3, leading to 2-aminothiazoles in a few minutes and high yields [46]:



Suzuki *et al.* [47] have reported the synthesis of 5-substituted aminothiazole-4-carboxylic acid by the treatment of methyl a-isocyanoacetate with a proper isothiocyanate in the presence of potassium tertiary butoxide in tetrahydrofuran (THF) at room temperature:

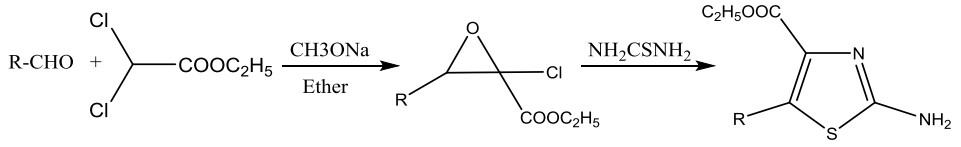


Alvarez Ibarra *et al.* [48] have further reported the synthesis of 2-etylthio-4-carbethoxy-5-alkyl/arylaminothiazoles by treatment of EMIC in the presence of potassium t-butoxide with isothiocyanate in THF:

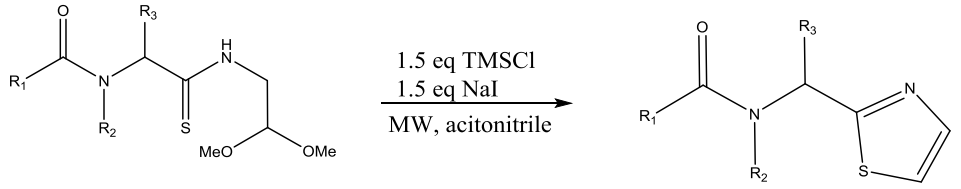


Where R= Ph, Et, n-Bu

Takeda *et al.* [49] have devised an ingenious method of synthesizing 2-amino-5-arylthiazole-4-carboxylates by the following:

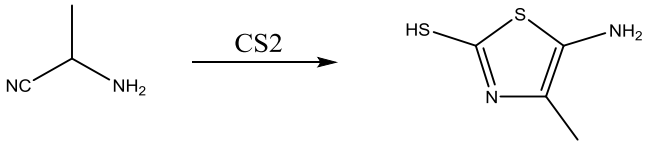


Uli Kazmaier *et al.* [50] have the synthesis of thiazole derivative by microwave to the TMSCl–NaI treatment gave the expected thiazoles in good to excellent yield:

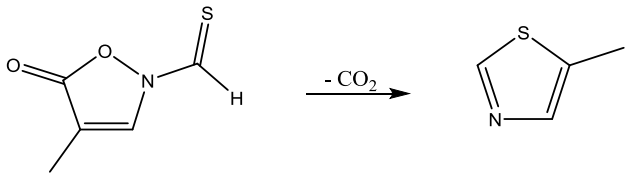


Direct conversion of endothiopeptides into thiazoles

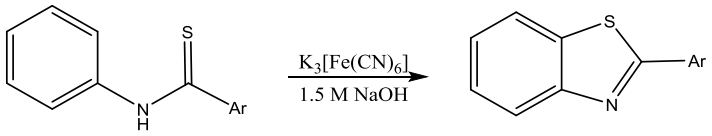
Cook–Heilbron synthesis is another versatile method for the synthesis of 2-aminothiazole from amino nitriles [51]:



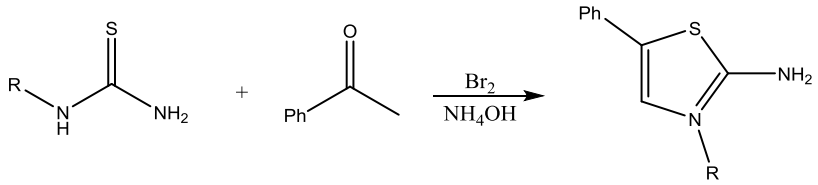
Thioacylisoxazol-5(2H)-ones undergo intramolecular cyclization of the iminocarbene to afford thiazoles under photochemical conditions [52]:



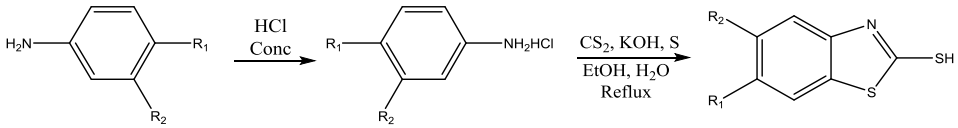
The Jacobson synthesis of benzothiazoles involves oxidative cyclization of an arylthioamide using potassium ferricynide in a basic medium [53]:



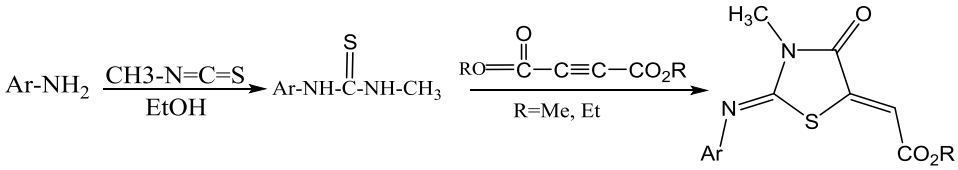
Another frequently used method for the synthesis of thiazoles involves the condensation of acetophenone with thiourea or a thioamide [54, 55]:



Sunil *et al.* [56] have the synthesis of benzthiazole derivatives by using a synthetic route given in scheme as follows:

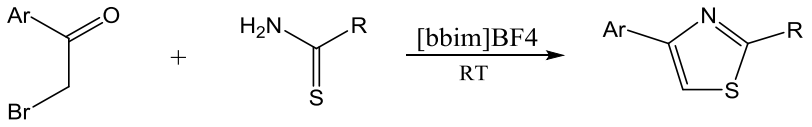


In the following reaction between activated acetylenic compounds and thiourea derivatives, which afforded 1.3-thiazolane derivatives in good isolated yields [57]:

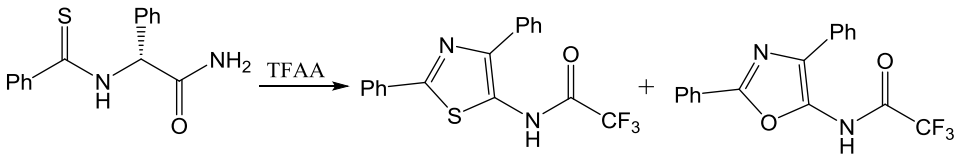


As a continuation of our research devoted to the development of green organic processes through performing reactions in green solvents such as ionic liquids, herein, we report a versatile [58] environmentally friendly synthesis of 2-amino-4-arylthiazole and 2-methyl-4-arylthiazole in ionic liquid (IL). The treatment of phenacyl

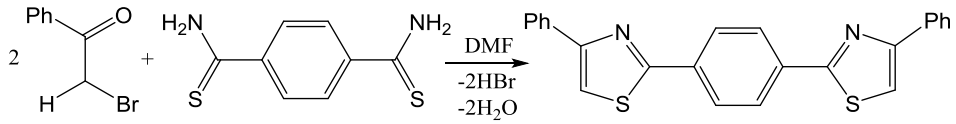
bromides and thiourea or thioamides in the IL 1,3-di-n-butylimidazolium tetrafluoroborate ([bbim]BF4) at ambient temperature afforded the corresponding 2-amino-4-arylthiazole and 2-methyl-4-arylthiazole derivative follows in excellent yields:



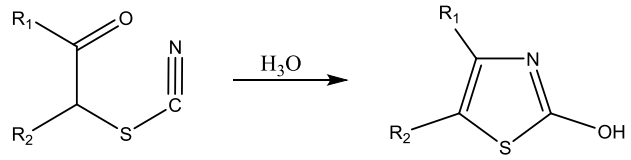
Our initial approach was based on the results of Barrett [59] who reported conversion of 2-N-(thiobenzoyl)acetamides into 5-(trifluoroacetylamino) thiazoles in good yields upon treatment with neat TFAA. The analogous reaction of 2-phenyl-2-(thiobenzoylamino)acetamide not a substrate investigated by Barrett was found to result in the formation of an approximately equal mixture of thiazole and oxazole. This problem of mixed product formation was overcome by reaction of the base compound with Lawesson's reagent prior to treatment with TFAA, resulting in exclusive formation of the desired thiazole product:



Thiazole derivative can be obtained by condensation of α-haloketone with dithioamide (2.4-disubstituted thiazoles). The cyclization of two moles of α-haloketone with dithioamide resulted in 1.4-bis(4-phenyl-2-thiazolyl) benzene in high yield [60]:

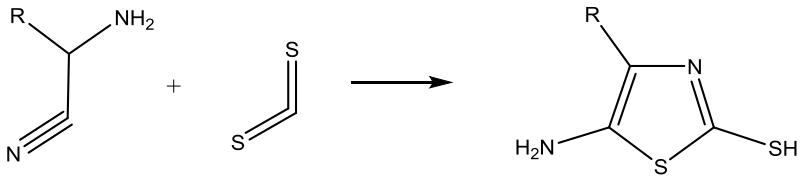


The cyclization of α-thiocyanatoketones in aqueous acid, concentrated sulphuric acid in acetic acid and water or alkaline solution leads to 2-hydroxy thiazoles after dilution in water [61]. These reactions can be carried out for several hours at room temperature or by heating for1 or 2 hrs on a steam bath:

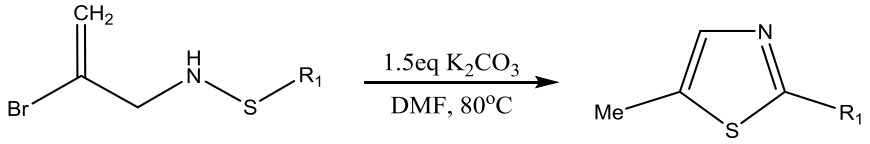


R_1,R_2= Alkyl, Phenyl

Carbon disulphide readily reacts with α-aminonitriles giving 2-mercapto-5-amino thiazoles [62], which can be converted to 5-amino thiazoles unsubstituted in the 2-position:



Thiazoles bearing a variety of substituents such as aliphatic, aromatic, heterocyclic, or alkenyl groups can be prepared by intramolecular nucleophilic substitution reaction of N-(2-bromoprop-2-enyl) thioamides [63]. This vinyl substitution method would provide unique synthetic route for a variety of heterocycles:



R_1= Aliphatic, aromatic, heterocyclic or alkyl groups

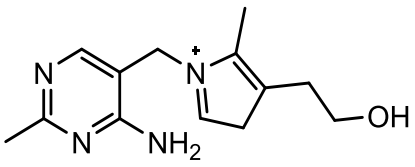
From the commercially available methyl benzoate derivatives and with racemic phenylglycine, a variety of 2,4-disubstituted-5-acetoxythiazoles were prepared in good to moderate yields using the following protocol [64]. Because of the high thermal stability of the thiazole nucleus, the polymers incorporating thiazole ring system have also been synthesized.

Thiamine is required for the biosynthesis of the neurotransmitters such as acetylcholine and gamma-amino butyric acid [66, 67]. Its deficiency results in Korsakoff syndrome, optic neuropathy and a disease called beriberi and confusion [68].

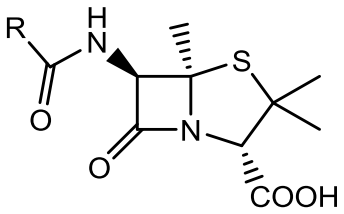
Penicillin G is a β-lactam antibiotic used in the treatment of bacterial infections caused by gram-positive bacteria [69].

Niridazole is used as schistosomicide [70] and is prescribed for the treatment of periodontitis (inflammatory disease) too [71, 72].

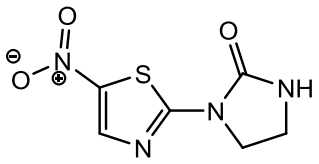
Fentiazac is a non-steroidal anti-inflammatory agent used for joint and muscular pain [73].



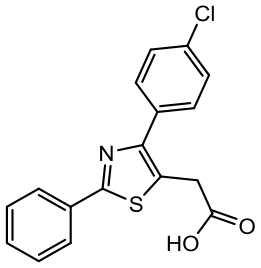
Thiamine



Penicillin G



Niridazole



Fentiazac

6. THIAZOLE DERIVATIVES UNDER THERAPEUTIC INVESTIGATION

6.1. Thiazole-Containing Compounds Endowed with Anticancer Activity

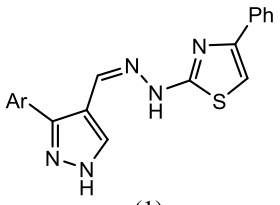
Thiazole and its derivatives are amongst most active classes of compounds that are known for their broad spectrum of activity e.g. antibacterial activity [74], antifungal activity [75], antimalarial activity [76], antitubercular activity [77], antiviral activity [78], anti-inflammatory activity [79], antidiabetic activity [80], anthelmintic activity [81], anticonvulsant activity [82], antioxidant activity [83], anticancer activity [84] and cardiovascular activity [85], *etc*. Moreover, thiazole-containing compounds have marked their presence in number of clinically available anticancer drugs (Fig) such as EGFR/VGFR kinase inhibitor, NF-KB inhibitor, CDC7 inhibitor and inhibitor of enzyme B-RAF [86], *etc*. Thiazole containing compounds depict anticancer activity profile through diverse mechanisms.

6.2. Antibacterial and Antifungal Agents

The resistance of pathogenic bacteria toward available drugs has been reported worldwide. Moreover, the incidence of fungal infections increased rapidly because of unselective antifungal activities and easily gained resistance. Therefore, the researches have been focused toward development of new antimicrobial agents with novel target [87]. In this way, different thiazole bearing compounds show promising antimicrobial activities. In the following sentences, we describe some molecules containing thiazole ring systems as novel antimicrobial agents [88].

In a study by Vijesh and co-workers [89], a series of 2,4-disubstituted thiazole Schiff bases (1) containing pyrazole moiety was synthesized by the Vilsmayer–Haack reaction of appropriate

semi-carbazones [90]. All compounds were screened for their antibacterial activities against *S.aureus*, *B.subtilis*, *E.coli* and *P.aeruginosa* [91].



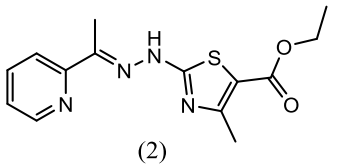
(1)

(1). Structure of thiazole antimicrobial agents.

6.3. Antitubercular Agents

Nowadays, the incidence of *Mycobacterium tuberculosis* infections is increasing very fast because of poverty and the HIV/AIDS pandemic. Thus, inefficiency of the conventional antitubercular drugs and appearance of multi-drug-resistant to various strains of *M.tuberculosis*, are the main problems [92–94]. Among antitubercular agents, some thiazole bearing compounds showed promising antitubercular activities.

In a study by Makam and co-workers, a series of 2-(2-hydrazinyl)thiazole derivatives were synthesized and evaluated against *Mycobacterium tuberculosis*. Among the synthesized compounds, ethyl-4-methyl-2-[(E)-2-[1-(pyridin-2-yl)ethylidene]hydrazin-1-yl]-1.3-thiazole-5-carboxylate (2) showed noticeable inhibitory activity against *M.tuberculosis* [95]:



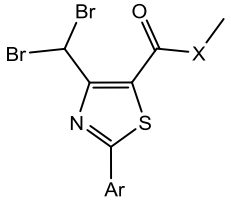
(2)

(2). Thiazole-based compound with antitubercular activity.

6.4. Antiviral Agents

Viral infections are considered as one of the most common and dangerous diseases which kill many people annually [96]. Besides recent advances in the field of antiviral drugs, there is emergency need to find more effective and efficient agents yet. In this field, many thiazole-based compounds were synthesized and evaluated that some of them are reported here. A new generation of methyl 4-(dibromomethyl)-2-(4-chlorophenyl)thiazole-5-carboxylate (3), which

was the most potent derivative among the primary compounds, have been synthesized and tested by Mayhoub *et al.* against yellow fever virus using a cell-based assay **[97]:**



X= O, CH_2, N, S

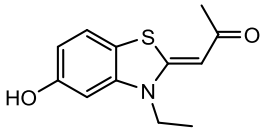
(3)

(3). Structure of some thiazole derivatives as antiviral agents.

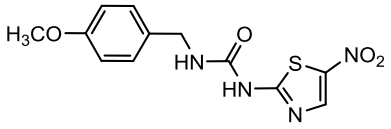
6.5. Anti-Alzheimer's Agents

The novel benzothiazole fully blocks the dual specific tyrosine phosphorylation regulated **(4) [98].** The non-carboxylic acid imidazole derivatives exhibited strong inhibition of plaque deposition **[99].**

(5) was reported as Alzheimer's diseases-related glycogen synthase kinase inhibitor, which prevented neurological mitochondrial apoptosis and reduced inflammation **[100, 101].**



(4)

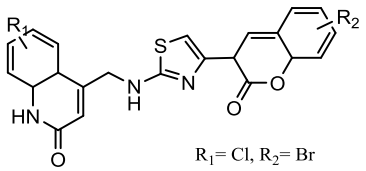


(5)

(4), (5). Thiazole derivatives as treatment of Alzheimer's disease.

6.6. Anti-Inflammatory Agents

Kalkhambkar *et al.* have synthesized triheterocyclic thiazole derivatives **(6)** and evaluated for their *in vivo* analgesic (inhibition up to 88% and 78%), and anti-inflammatory potential (inhibition up to 29% to 42%) **[102]:**



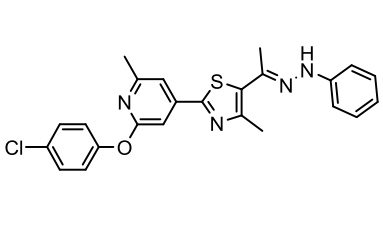
R_1= Cl, R_2= Br

(6)

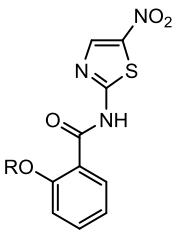
(6). Thiazole derivative designed as anti-inflammatory agents.

6.7. Antiviral Agents

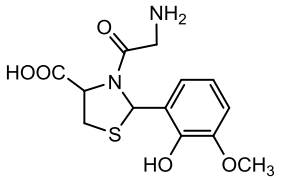
Kampmann *et al.* have reported thiazole derivative (7), which inhibited dengue virus (DENV), envelope proteins [103]. A series of thiazole containing benzo[*d*]isothiazol-3-(2H)-one derivatives (8) were identified as inhibitors of DENV2 [104]. Liy *et al.* have synthesized thiazolidines (9) for inhibiting influenza A neuraminidase enzyme [105, 106].



(7)



(8)

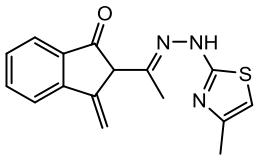


(9)

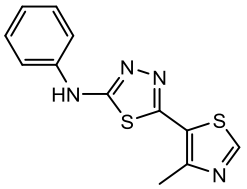
(7), (8), (9). Structures of some thiazole derivatives as antiviral agents.

6.8. Antimicrobial Agents

Rajni *et al.* have synthesized some thiazole derivatives (10) with potent antimicrobial activity against *S. aureus*, *B.subtilis* and *E.coli* [107]. Karale *et al.* have synthesized (11) and evaluated them against *B.subtilis*, *S.aureus* and *E.coli* [108]. Compound containing catechol unit improved Gram-negative inhibition [109].



(10)



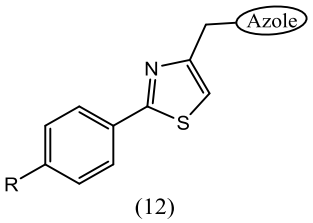
(11)

(10), (11). Structures of some thiazole derivatives as antimicrobial agents

6.9. Anticonvulsant Agents

Epilepsy is characterized by abnormal and excessive discharge of neurons that cause loss or disturbances of consciousness, with or without characteristic body movements [110]. Commercially available anticonvulsant drugs can control the seizures in only less than 70% of patients. Inefficiency of drugs and their undesirable side effects such as ataxia, headache, and anaemia show the necessity for search novel antiepileptic agents with more selectivity and lower

toxicity in medicinal chemistry [111, 112]. In the field of anticonvulsant agents, many compounds are found with thiazole scaffold, which several of them are described here. A series of novel 1-[(2-arylthiazol-4-yl)methyl] azoles were synthesized and screened for their anticonvulsant properties by Emami *et al.* in 2011. Anticonvulsant activity of synthesized compounds was tested by using two models, PTZ and MES in mice. Among the target compounds, imidazol derivative, 1-[(2-(4-chlorophenyl) thiazol-4-yl) methyl]-1H-imidazole and triazolyl derivative, 1-[(2-phenylthiazol-4-yl)methyl]-1H-1,2,4-triazole and its 4-chlorophenyl analog showed the highest anticonvulsant activity in both models with percentage protection range of 33–100%. The structure-activity relationship and drug-likeness studies revealed that thiazole-incorporated (arylalkyl)azoles which showed good protection in both models of epilepsy (PTZ and MES) can be regarded as promising candidate for future investigations [113, 114]:



(12)

(12). Structure of some thiazole derivatives with anticonvulsant activity.

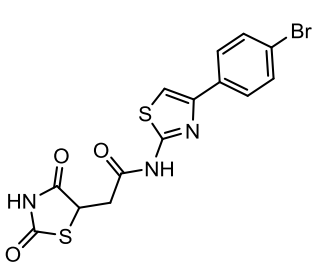
6.10. Antioxidant Agents

Increased the level of reactive oxygen species (ROS) under free radical oxidative stress condition causes some damages in cell growth, gene expression and host defence. Therefore, controlling the level of free radicals in cells seems to be essential to decrease damages [115].

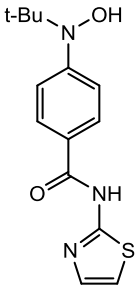
The antioxidant activity of 2,4-dioxo-1,3-thiazolidine thiazoles have been studied by Yadla team using DPPH method. Based on their report, para-bromo derivative 13 showed the highest antioxidant potency, comparable to ascorbic acid and luteolin as reference compounds [116].

In order to find new therapeutic agents for treatment of neurodegenerative disorders, Kim *et al.* designed novel antioxidant 14 containing N-t-butyl-N hydroxyl aminophenyl moiety. The N-t-butyl-N-hydroxyl amino phenyl scaffold could have potential antioxidant activity because of high stability of radical species generated from abstraction of hydrogen on N–OH by reactive oxygen species (ROS). This study has indicated that thiazole-possessing compound

14 remarkably decreased the neurotoxicity induced by ROS at 10 μM concentrations. In addition, the mentioned compound showed the best lipid peroxidation (LPO) inhibition and *in vivo* neuroprotective activities using gerbils as animal models [117, 118]:



(13)



(14)

(13), (14). Thiazole derivatives and related compounds reported as antioxidant agents.

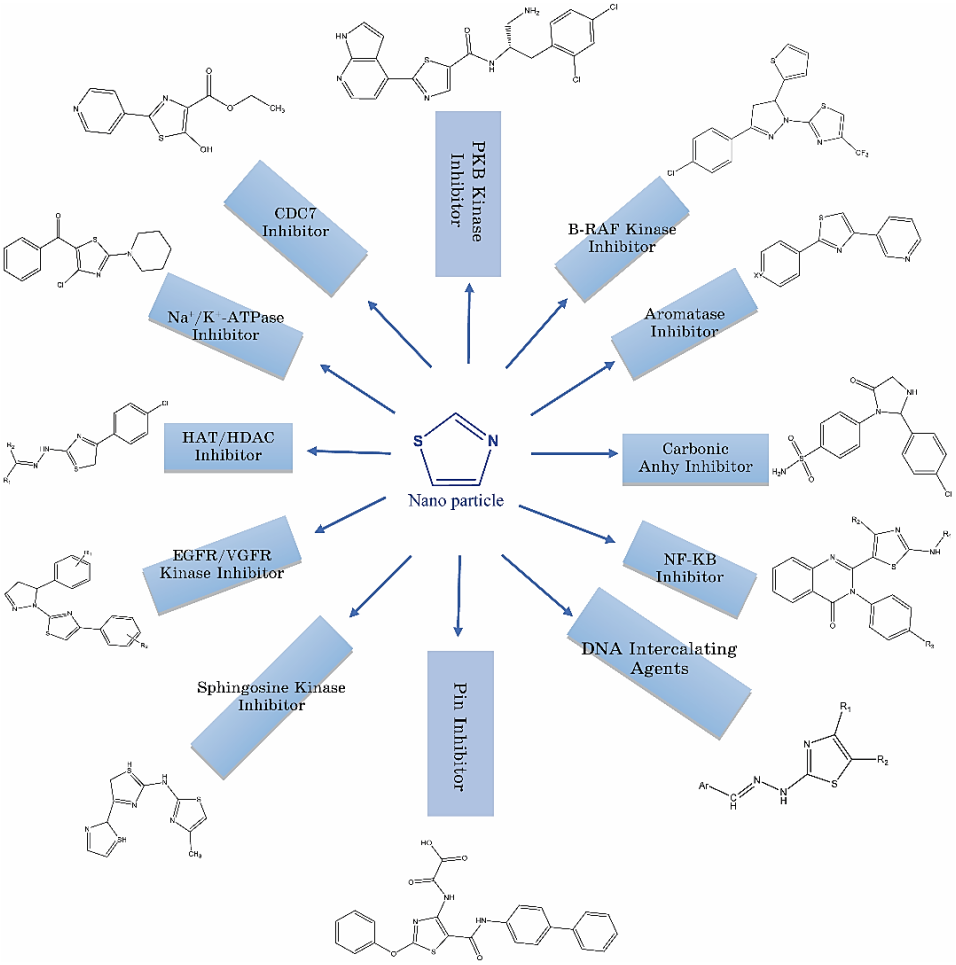
7. CONCLUSION

The current review emphasizes on new horizons of anticancer potential of thiazole nanoparticles based heterocyclic derivatives. Thiazoles are a unique moiety that is responsible for various biological activities and is found in many famous drugs such as penicillin, nitazoxanide, bleomycin, meloxicam, fentiazac, tiazofurin, ritonavir, *etc*.

Besides this, we have mainly focused on different series of thiazole derivatives with diverse biological activities including antibacterial, antifungal, antitubercular, anticancer, anticonvulsant, anti-inflammatory, and antioxidant.

In addition, we have discussed a few methods of synthesis of thiazole derivatives and some therapeutic drugs bearing the thiazole nucleus. This has been noticed so far that modifications on thiazole moiety results in the formation of compounds with valuable biological activities. It will be interesting to observe that these modifications can be utilized as potent therapeutic agents in future. Moreover, several thiazole-based enzyme inhibitors, which may be useful for treatment of Alzheimer's disease, diabetes, gout and other chronic diseases, are also highlighted.

This article helps to find potential future directions on the development of more potent and specific analogs of thiazole-based compounds for various biological targets. Development of superior analogs with better efficacy and pharmacokinetics and less side effects would be incredible contribution for the betterment of human beings.



Thiazoles as multitargeting agents in cancer.

REFERENCES

1. R. M. Achson, *An Introduction to the Chemistry of Heterocyclic Compounds* (India: Willy-Intersciences: 2009), p. 1375.
2. P. S. Yadav, D. Prakash, and G. P. Senthilkumar, *International Journal of Pharmaceutical Sciences and Drug Research*, **3**, No. 1: 1 (2011).
3. K. M. Khan, S. Qurban, U. Salar, and M. Taha, *Bioorganic Chemistry*, **68**, No. 245: 58 (2016); http://doi:10.1016/j.bioorg.2016.08.010
4. S. K. Nirav, S. M. Nimesh, P. P. Manish, and P. G. Ranjan, *Journal of the Serbian Chemical Society*, **77**, Iss. 3: 279 (2012); https://doi.org/10.2298/JSC110630197S
5. A. K. Prajapati and V. P. Modi, *Quim. Nova*, **34**, No. 5: 64 (2011); https://doi.org/10.1590/S0100-40422011000500008

6. A. Colon, T. J. Hoffman, J. Gebauer, J. Dash, J. H. Rigby, S. Arseniyadis, and J. Cossy, *F. Chem. Commun.*, **48**, Iss. 8: 10508 (2012); https://doi.org/10.1039/C2CC35721F
7. J. M. Clough, H. Dube, B. J. Martin, G. Pattenden, K. S. Reddy, and I. R. Waldron, *Org. Biomol. Chem.*, **4**, Iss. 15: 2906 (2006); https://doi.org/10.1039/B603433K
8. J. W. Ahn, S. H. Woo, C. O. Lee, K. Y. Cho, and B. S. Kim, *J. Nat. Prod.*, **62**, Iss. 3: 495 (1999); https://doi:10.1021/np9804233
9. H. Steinmetz, E. Forche, H. Reichenbach, and G. Höfle, *Tetrahedron*, **56**, Iss. 12: 1681 (2000); https://doi.org/10.1016/S0040-4020(00)00063-6
10. G. P. Gunawardana, S. Kohmoto, S. P. Gunesakara, O. J. McConnel, and F. E. Koehn, *J. Am. Chem. Soc.*, **110**: 4856 (1988); https://doi.org/10.1021/ja00222a071
11. L. Feliu, W. Ajanaa, M. Alvarez, and J. A. Joule, *Tetrahedron Lett.*, **53**, Iss. 12: 4511 (1997); https://doi.org/10.1016/S0040-4020(97)00125-7
12. G. Chabowska, E. Barg, and A. Wyjcicka, *National Library of Medicine*, **26**, No. 14: 4324 (2021); https://doi:10.3390/molecules26144324
13. G. T. Zitouni, M. D. Altıntop, A. Özdemir, F. Demirci, U. A. Mohsen, and Z. A. Kaplancikli, *J. Enzyme Inhib. Med. Chem.*, **28**, No. 6: 1211 (2013); https://doi:10.3109/14756366.2012.723208
14. P. S. Yadav, D. Prakash, and G. P. Senthilkumar, *International Journal of Pharmaceutical Sciences and Drug Research*, **3**, No. 1: 1 (2011); https://doi:1025004
15. J. K. Malik, S. Singh, and P. Purohit, *Der Pharmacia Lettre*, **2**, No. 1: 347, (2010).
16. J. X. Mu, Y. X. Shi, H. K. Wu, Z. H. Sun, M. Y. Yang, X. H. Liu, and B. J. Li, *National Library of Medicine*, **10**, Iss. 50: 91 (2016); https://doi:10.1186/s13065-016-0196-6
17. F. Chadegani, F. Darviche, and S. Balalaie, *International Journal of Organic Chemistry*, **2**, No. 1: 31 (2012); https://doi:10.4236/ijoc.2012.21006
18. S. Bondock, W. Fadaly, and M. A. Metwally, *European Journal of Medicinal Chemistry*, **45**, Iss. 9: 3692 (2010); https://doi:10.1016/j.ejmech.2010.05.018
19. S. Pola, *Heterocycles from Organic and Pharmaceutical Perspective*, **21**: 106 (2009); https://doi:10.5772/62077
20. A. M. Ali, G. E. Saber, N. M. Mahfouz, M. A. El-Gendy, A. A. Radwan, and M. A. Hamid, *Archives of Pharmacial Research*, **30**: 1186 (2007); http://doi.org/10.1007/BF02980259
21. J. V. Metzger, *The Chemistry of Heterocyclic Compounds — Thiazole and Its Derivatives* (New York: John Wiley & Sons Inc.: 2007), vol. **34**, part 1.
22. A. A. Geronikaki, A. A. Lagunin, D. H. Litina, P. T. Eleftheriou, D. A. Filimonov, V. V. Poroikov, I. Alam, and A. K. Saxena, *J. Med. Chem.*, **51**, No. 6: 1601 (2008); https://doi.org/10.1021/jm701496h
23. A. H. Abdelazeem, S. I. Khan, S. W. White, K. J. Sufka, C. R. McCurdy, *Bioorganic & Medicinal Chemistry*, **23**, Iss. 13: 3248 (2015); https://doi.org/10.1016/j.bmc.2015.04.057
24. A. U. Malgorzata, X. Zhang, and S. Prakash, *Cell Biochemistry and Biophysics*, **72**, No. 3: 86 (2015); https://doi.org/10.1007/s12013-015-0528-5
25. P. Yer, J. Bolla, V. Kumar, M. S. Gill, and M. E. Sobhia, *Molecular Diversity*, **19**, No. 4: 855 (2015); https://doi.org/10.1007/s11030-015-9578-2

26. Y. Ali, M. S. Alam, H. Hamid, A. Husain, A. Dhulap, F. Hussain, S. Bano, and C. Kharbanda, *New Journal of Chemistry*, **40**, No. 1: 711 (2016); https://doi.org/10.1039/C5NJ00078E
27. A. El-Mekabaty, M. O. Osman, O. O. Habib, B. M. Evelin, and A. M. Hasel, *Journal of Heterocyclic Chemistry*, **53**, No. 4: 106 (2016); https://doi.org/10.1002/jhet.2412
28. R. S. Keri, M. R. Patil, S. A. Patil, and S. Budagumpi, *Eur. J. Med. Chem.*, **89**: 207 (2015); https://doi:10.1016/j.ejmech.2014.10.059
29. S. J. Kashyap, V. K. Garg, P. K. Sharma, N. Kumar, R. Dudhe, and J. K. Gupta, *Medicinal Chemistry Research*, **21**: 2123 (2012); https://doi.org/10.1007/s00044-011-9685-2
30. I. I. Ilkiv, R. B. Lesyk, and O. Y. Sklyarov, *The Ukrainian Biochemical Journal*, **88**: 99 (2016); https://doi.org/10.15407/ubj88.si01.099
31. D. P. Gouvea, F. A. Vasconcellos, G. D. Anjos, A. C. Pinto, S. Neto, G. Fischer, R. P. Sakata, W. P. Almeida, and W. Cunico, *European Journal of Medicinal Chemistry*, **118**: 1075 (2016); https://doi.org/10.1016/j.ejmech.2016.04.028
32. A. M. Abdel-Aziz, L. A. Abou-Zeid, K. E. ElTahir, M. A. Mohamed, M. A. Abu El-Enin, A. S. El-Azab, *Bioorganic & Medicinal Chemistry*, **24**, No. 16: 48 (2016); https://doi.org/10.1016/j.bmc.2016.06.026
33. A. Lozynskyi, S. Golota, B. Zimenkovsky, D. Atamanyuk, A. Gzella, and R. Lesyk, *Phosphorus, Sulfur, and Silicon and the Related Elements*, **191**, No. 9: 1245 (2016); https://doi.org/10.1080/10426507.2016.1166108
34. M. Arfeen, S. Bhagat, R. Patel, S. Prasad, I. Roy, K. A. Chakraborti, and P. V. Bharatam, *European Journal of Medicinal Chemistry*, **121**: 942 (2016); https://doi.org/10.1016/j.ejmech.2016.04.075
35. K. Appalanaidu, R. Kotcherlakota, T. L. Dadmal, V. S. Bollu, R. M. Kumbhare, and C. R. Patra, *Bioorganic & Medicinal Chemistry Letters*, **26**, No. 21: 317 (2016); https://doi.org/10.1016/j.bmcl.2016.08.013
36. A. El-Mekabaty, M. Osman, O. Habib, E. B. Moawad, and A. M. Hasel, *Journal of Heterocyclic Chemistry*, **53**, No. 6: 421 (2016); https://doi.org/10.1002/jhet.2492
37. A. Abdelmajeid, M. S. Amine, and R. A. Hassan, *International Journal of Organic Chemistry*, **07**, No. 4: 1 (2017); https://doi.org/10.4236/ijoc.2017.74029
38. A. A. Fedorchuk, V. V. Kinzhybalo, Yu. I. Slyvka, E. A. Goreshnik, T. J. Bednarchuk, T. Lis, and M. G. Mys'kiv, *Journal of Coordination Chemistry*, **70**, No. 5: 71 (2017); https://doi.org/10.1080/00958972.2017.1286012
39. H. A. Abd El Razik, M. H. Badr, A. H. Atta, S. M. Mouneir, and M. M. Abu-Serie, *Archiv der Pharmazie*, **350**, No. 5: 353 (2017); https://doi.org/10.1002/ardp.201700026
40. D. Kaminskyy, A. Kryshchyshyn, and R. Lesyk, *European Journal of Medicinal Chemistry*, **140**: 137 (2017); https://doi.org/10.1016/j.ejmech.2017.09.031
41. H. S. Arthur, S. D. Daniel, M. G. Siqueira, G. D. Gamaro, W. Cunico, and L. D. Adriana, *Medicinal Chemistry Research*, **27**, No. 1: 124 (2018); https://doi.org/10.1007/s00044-017-2052-1
42. T. M. Potewar and S. Ingale, *Tetrahedron*, **63**: 11066 (2007); https://doi.org/10.1016/J.TET.2007.08.036
43. S. B. Yoon, E. J. Chun, Y. R. Noh, Y. J. Yoon, and S. G. Lee, *Bulletin of*

the Korean Chemical Society, **34**, Iss. 9: 321 (2013); https://doi.org/10.5012/bkcs.2013.34.9.2819
44. M. Alam, S. Khan, and M. S. Khan, *Journal of the Chilean Chemical Society*, **53**, No. 4: 421 (2008); http://doi.org/10.4067/S0717-97072008000400017
45. A. H. Cook, I. Heilbron, S. F. MacDonald, and A. P. Mahadevan, *J. Chemical Society*, **12**: 1064 (1949); https://doi.org/10.1039/JR9490001064
46. G. S. Lingaraju, T. R. Swaroop, A. C. Vinayaka, K. S. S. Kumar, M. P. Sadashiva, and K. S. Ragappa, *Tetrahedron*, **44**: 1373 (2012); https://doi.org/10.1055/s-0031-1290762
47. A. A. Hassan, N. K. Mohamed, K. M. El-Shaieb, H. N. Tawfeek, and S. B. Nieger, *Arabian Journal of Chemistry*, **12**, Iss. 2: 39 (2019); https://doi.org/10.1016/j.arabjc.2014.10.035
48. T. J. Rashamuse, M. Q. Fish, E. M. Coyanis, and M. L. Bode, *Integrase Interaction Inhibitors*, **26**, No. 20: 104242 (2021); https://doi.org/10.3390/molecules26206203
49. C. A. Ganou, P. Th. Eleftheriou, P. Theodosis-Nobelos, M. Fesatidou, A. A. Geronikaki, T. Lialiaris, and E. A. Rekka, *SAR and QSAR in Environmental Research,* **29**, No. 2: 133 (2018); https://doi.org/10.1080/1062936X.2017.1414874
50. O. Kouatly, Ph. Eleftheriou, A. Petrou, D. Hadjipavlou-Litina, and A. Geronikaki, *SAR and QSAR in Environmental Research*, **29**, No. 2: 1601 (2018); https://doi.org/10.1080/1062936X.2017.1410220
51. B. Qi, Y. Yang, H. He, X. Yue, Y. Zhou, X. Zhou, Y. Chen, M. Liu, A. Zhang, and F. Wei, *European Journal of Medicinal Chemistry*, **146**: 112001 (2018); https://doi.org/10.1016/j.ejmech.2018.01.061
52. K. Liaras, M. Fesatidou, and A. Geronikaki, *Molecules*, **23**, No. 3: 685 (2018); https://doi.org/10.3390/molecules23030685
53. R. H. Prager, M. R. Taylor, and C. M. Williams, *J. Chem. Soc. Perkin Trans.*, **1**: 79 (1997).
54. N. K. Downer and Y. A. Jackson, *Organic. Biomorganic. Chemistry*, **2**: 49 (2004); https://doi.org/10.1039/B410373D
55. S. A. Ibrahim and H. F. Rizk, *J. Chem. Soc. Perkin Trans.*, **1**, No. 96: 4093 (1998).
56. V. E. Borisenko, A. Koll, E. E. Kolmakov, and A. G. Rjasnyi, *Journal of Molecular Structure*, **783**: 75 (2006).
57. S. Kumar, D. S. Rathore, G. Garg, K. Khatri, R. Saxena, and S. K. Sahu, *International Journal of Pharmacy and Pharmaceutical Sciences*, **9**, Iss. 2: 147 (2017); https://doi.org/10.22159/ijpps.2017v9i2.14359
58. A. Doregiraee, E. T. Kermani, H. Khabazzadeh, and P. Pouramiri, *J. Chil. Chem. Soc.*, **60**, No. 3: 374 (2015); http://doi.org/10.4067/S0717-97072015000300009
59. T. M. Potewar and S. A. Ingale, *Tetrahedron*, **63**, No. 45: 479 (2007); http:/.doi.org/10.1016/j.tet.2007.08.036
60. Mark J. Thompson, William Heal, and Beining Chen, *Tetrahedron Letters*, **47**, Iss. 14: 2361 (2006); https://doi.org/10.1016/j.tetlet.2006.02.004
61. A. Mori, A. Sekiguchi, K. Masui, T. Shimada, M. Horie, K. Osakada et al., *Journal of the American Chemical Society*, **125**, No. 7: 1700 (2003); https://doi.org/10.1021/ja0289189
62. B. Y. Kim, H. S. Kim, and A. A. Helal, *Sensors and Actuators B: Chemical*,

206: 430 (2015); https://doi.org/10.1016/j.snb.2014.09.071
63. T. Bach and S. Heuser, *Tetrahedron Letters*, **41**, Iss. 11: 1707 (2000); https://doi.org/10.1016/S0040-4039(00)00018-6
64. A. Dondoni, *Organic & Biomolecular Chemistry*, **8**: 3366 (2010); https://doi.org/10.1039/C002586K
65. Xugang Guo, Jordan Quinn, Zhihua Chen, Hakan Usta, Yan Zheng, Yu Xia, Jonathan W. Hennek, Rocно Ponce Ortiz, Tobin J. Marks, and Antonio Facchetti, *J. Am. Chem. Soc.*, **135**: 1986 (2013); https://doi.org/10.1021/ja3120532
66. W. C. Patt, W. C. Hamilton, M. D. Taylor, M. J. Ryan, C. J. Connolly, S. P. Klutchko, I. Sirear, B. L. Batley, S. T. Rapundalo, and S. C. Olson, *J. Med. Chem.*, **35**, No. 14: 2562 (1992); https://doi.org/10.1021/jm00092a006
67. R. A. Peters, *Lancet*, **5882**: 1161 (1936).
68. R. Breslow, *J. Am. Chem. Soc.*, **80**, No. 14: 12590 (1958).
69. J. J. Kril, *Metab. Brain. Dis.*, **11**, No. 1: 19 (2006); https://doi.org/10.1007/BF02080928
70. L. P. Garrod, *Br. Med. J.*, **1**, No. 5172: 1201 (1960); https://doi:.org/10.1136/bmj.1.5172.527
71. J. W. Tracy, B. A. Catto, and L. T. Webster, *Mol. Pharmacol.*, **24**, No. 2: 54 (1983).
72. R. Barat, A. Srinatha, J. Pandit, N. Mittal, and S. Anupurba, *Drug Delivery*, **14**, No. 8: 87 (2007); https://doi.org/10.1080/10717540701606517
73. R. Barat, A. Srinatha, J. K. Pandit, D. Ridhurkar, J. Balasubramaniam, N. Mittal, and D. N. Mishra, *Drug Delivery*, **13**, Iss. 5: 645 (2008); https://doi.org/10.1080/10717540500398126
74. T. Moulard, J. F. Lagorce, J. C. Thomas, and C. Raby, *J. Pharm. Pharmacol.*, **24**, No. 8: 147 (1993); https://doi.org/10.1111/j.2042-7158.1993.tb07098.x
75. B. Ghasemi, G. Sanjarani, Z. Sanjarani, and H. Majidiani, *Iran. J. Microbiol.*, **7**, No. 5: 281 (2015).
76. S. Khabnadideh, Z. Rezaei, K. Pakshir, K. Zomorodian, and N. Ghafari, *Res. Pharm. Sci.*, **7**, No. 2: 65 (2012).
77. J. M. Bueno, M. Carda, B. Crespo, A. C. Cunat, C. de Cozar, M. L. Leon, J. A. Marco, N. Roda, and J. F. Sanz-Cervera, *Bio Org. Med. Chem. Lett.*, **26**: 102914 (2016).
78. A. M. Alqahtania and A. A. Bayazeed, *Arabian Journal of Chemistry*, **14**, Iss. 1: 241 (2021); https://doi.org/10.1016/j.arabjc.2020.11.020
79. K. W. Dawood, T. M. Eldebss, H. S. El-Zahabi, and M. H. Yousef, *Eur. J. Med. Chem.*, **18**, No. 102: 111 (2015); https://doi.org/10.1016/j.ejmech.2015.08.005
80. R. N. Sharma, F. P. Xavier, K. K. Vasu, S. C. Chaturvedi, and S. S. Pancholi, *Journal of Enzyme Inhibition and Medicinal Chemistry*, **24**, No. 3: 2029 (2009); https://doi.org/10.1080/14756360802519558
81. O. B. Dundar, M. C. Unlusoy, E. J. Verspohl, and R. Ertan, *Arzneimittelforschung*, **56**, No. 9: 264 (2006); https://doi.org/10.1055/s-0031-1296762
82. R. J. Weikert, S. J. Bingham, M. A. Emanuel, E. B. Smith, D. G. Loughhead, P. H. Nelson, and A. L. Poulton, *J. Med. Chem.*, **34**: 744 (1991).
83. K. V. Derpoorten, H. Ucar, and Poupaert, *J. Med. Chem.*, **41**: 671 (1998).
84. B. Z. Kurt, I. Gazioglu, F. Sonmez, and M. Kucukislamoglu, *Bio. Org. Chem.*, **59**: 11 (2015); https://doi.org/10.1016/j.bioorg.2015.02.002

85. A. Lozynskyi, B. Zimenkovsky, and R. Lesyk, *Sci. Pharm.*, **82**, No. 4: 723 (2014); https://doi.org/10.3797/scipharm.1408-05
86. A. M. Omar and N. H. Eshba, *J. Pharm. Sci.*, **73**, No. 8: 440 (1984); https://doi.org/10.1002/jps.2600730837
87. S. Hu-Lieskovan, S. Mok, B. Homet Moreno, J. Tsoi, L. Robert, L. Goedert, E. M. Pinheiro, R. C. Koya, T. G. Graeber, B. Comin-Anduix, and A. Ribas, *Sci. Transl. Med.*, **18**: 28502 (2015).
88. A. Geronikaki, P. Eleftheriou, P. Vicini, I. Alam, A. Dixit, and A. K. Saxena, *Journal of Medicinal Chemistry*, **51**, No. 17: 5221 (2008); https://doi.org/10.1021/jm8004306
89. M. Mishchenko, S. Shtrygol, A. Lozynskyi, M. Hoidyk, D. Khyluk, T. Gorbach, and R. Lesyk, *Scientia Pharmaceutica*, **90**, No. 3: 56 (2022); https://doi.org/10.3390/scipharm90030056
90. B. T. Harshitha, J. Jayashankar, A. P. Anand, S. Sandeep, H. S. Jayanth, C. S. Karthik, P. Mallu, N. Haraprasad, and N. B. Krishnamurthy, *Asian Journal of Chemistry*, **34**, No. 8: 2562 (2022); https://doi.org/10.14233/ajchem.2022.23673
91. L. H. Abdel-Rahman, S. K. Mohamed, Y. El Bakri, S. Ahmad, C. Lai, A. A. Amer, J. T. Mague, and E. M. Abdalla, *Journal of Molecular Structure*, **1245**: 165 (2021); https://doi.org/10.1016/j.molstruc.2021.130997
92. S. Badr, *Turkish Journal of Chemistry*, **35**, Iss. 1: 131 (2011).
93. C. Tratrat, M. Haroun, E. Tsolaki, A. Petrou, A. Gavalas, A. Geronikaki, *Current Topics in Medicinal Chemistry*, **21**, No. 4: 257 (2021); https://doi.org/10.2174/1568026621999201214232458
94. L. Y. He, S. S. Zhang, D. X. Peng, L. P. Guan, and S. H. Wang, *Bioorganic & Medicinal Chemistry Letters,* **30**, No. 17: 105 (2020); https://doi.org/10.1016/j.bmcl.2020.127376
95. V. J. Faldu, P. K. Talpara, N. H. Bhuva, P. R. Vachharajani, and V. H. Shah, *International Letters of Chemistry, Physics and Astronomy,* **25**: 26 (2014); https://doi.org/10.18052/www.scipress.com/ILCPA.25.26
96. C. Tratrat, *Combinatorial Chemistry & High Throughput Screening*, **23**, No. 2: 126 (2020); https://doi.org/10.2174/1386207323666200127115238
97. N. Sahiba, A. Sethiya, J. Soni, D. K. Agarwal, and S. Agarwal, *Topics in Current Chemistry*, **378**, No. 2: 34 (2020); https://doi.org/10.1007/s41061-020-0298-4
98. J. F. Rossignol, *Antiviral Research*, **110**: 94 (2014); https://doi.org/10.1016/j.antiviral.2014.07.014
99. Y. Ogawa, Y. Nonaka, T. Goto, E. Ohnishi, T. Hiramatsu et al., *Nat. Commun.*, **86**, No. 1: 1090 (2010); https://doi.org/10.1038/ncomms1090
100. M. Z. Kounnas, A. M. Danks, S. Comer et al., *Bio Org. Med. Chem. Lett.*, **67**, No. 5: 93 (2010); https://doi.org/10.1016/j.neuron.2010.08.018
101. S. M. Holota, H. O. Derkach, I. L. Demchuk, R. B. Vynnytska, O. I. Antoniv, L. O. Furdychko, N. Y. Slyvka, I. O. Nektegayev, and R. B. Lesyk, *Biopolymers and Cell*, **35**, No. 6: 81 (2019); https://doi.org/10.7124/bc.000A17
102. V. V. Poroikov, D. A. Filimonov, T. A. Gloriozova, A. A. Lagunin, D. S. Druzhilovskiy, A. V. Rudik, L. A. Stolbov, A. V. Dmitriev, O. A. Tarasova, S. M. Ivanov, and P. V. Pogodin, *Russian Chemical Bulletin*, **68**, No. 12: 8 (2019); https://doi.org/10.1007/s11172-019-2683-0

103. R. G. Kalkhambkar, G. M. Kulkarni, H. Shivkumar, and R. Nagendra Rao, *Eur. J. Med. Chem.*, **42**, Iss. 10: 1272 (2007); https://doi.org/10.1016/j.ejmech.2007.01.023
104. T. Kampmann, R. Yennamalli, D. P. Fairlie, B. Kobe, and P. R. Young, *Antiviral Res.*, **84**, No. 3: 443 (2009); https://doi.org/10.1016/j.antiviral.2009.09.007
105. K. C. Tiew, D. Dou, T. Teramoto, H. Lai, and K. R. Alliston, *Bioorg. Med. Chem.*, **20**, No. 3: 605 (2012); https://doi.org/10.1016/j.bmc.2011.12.047
106. T. Lin, O. Lenz, G. Fanning, T. Verbinnen, F. Delouvroy et al., *Antimicrob. Agents Chemother.*, **53**, No. 4: 1377 (2009); https://doi.org/10.1128/AAC.01058-08
107. Y. Liu, F. Jing, Y. Xu, Y. Xie, F. Shi, H. Fang, M. Li, and W. Xu, *Bioorg. Med. Chem.*, **19**, No. 7: 2342 (2011); https://doi.org/10.1016/j.bmc.2011.02.019
108. R. Mohil, D. Kumar, and S. Mor, *J. Hetrocyclic Chem.*, **51**, Iss. 1: 9 (2014); https://doi.org/10.1002/jhet.1081
109. Jitendra Nalawade, Abhijit Shinde, Abhijit Chavan, Sachin Patil, Manjusha Suryavanshi, Manisha Modak, Prafulla Choudhari, Vivek D. Bobade, and Pravin C. Mhaske, *European Journal of Medicinal Chemistry*, **179**: 649 (2019); doi:10.1016/j.ejmech.2019.06.074
110. R. P. Singh, M. N. Aziz, D. Gout, W. Fayad, M. A. El-Manawaty, and C. J. Lovely, *Bioorganic & Medicinal Chemistry*, **27**, No. 20: 167 (2019); https://doi.org/10.1016/j.bmc.2019.115047
111. V. Šlachtová, L. Janovská, and L. Brulíková, *Journal of Molecular Structure*, **1183**: 10118 (2019); https://doi.org/10.1016/j.molstruc.2019.01.073
112. Y. M. Omar, H. M. Abdu-Allah, G. Samia, and G. Abdel-Moty, *Bioorganic Chemistry*, **80**: 375 (2018); https://doi.org/10.1016/j.bioorg.2018.06.036
113. K. Liaras, M. Fesatidou, and A. Geronikaki, *Molecules*, **23**, No. 3: 685 (2018); https://doi.org/10.3390/molecules23030685
114. C. A. Ganou, P. Th. Eleftheriou, P. Theodosis-Nobelos, M. Fesatidou, A. A. Geronikaki, T. Lialiaris, and E. A. Rekka, *SAR and QSAR in Environmental Research*, **29**, No. 2: 133 (2018); https://doi.org/10.1080/1062936X.2017.1414874
115. D. Kaminskyy, A. Kryshchyshyn, and R. Lesyk, *European Journal of Medicinal Chemistry*, **140**: 490 (2017); https://doi.org/10.1016/j.ejmech.2017.09.031
116. I. I. Ilkiv, R. B. Lesyk, and O. Ya. Sklyarov, *The Ukrainian Biochemical Journal*, **88**: 99 (2016); https://doi.org/10.15407/ubj88.si01.099
117. F. Aksakal, N. Shvets, and A. Dimoglo, *Journal of Molecular Graphics and Modelling*, **60**: 1693 (2015); https://doi.org/10.1016/j.jmgm.2015.06.006
118. W. A. Bayoumi, S. H. Abdel-Rhman, and M. E. Shaker, *Open Chemistry Journal*, **1**, No. 1: 134 (2014); https://doi.org/10.2174/1874842201401010033