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Review Article

Current Synthesis Routes of Thiazole and its Derivatives and their Broad-Spectrum Therapeutic Activity

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Abstract: Thiazole is an important nucleus owing to its wide range of medical uses. It contains components that are anti-bacterial, anti-fungal, anti-malarial, anti-cancer, anti-allergic, anti-hypertensive, anti-inflammatory, anti-psychotic, as well as antioxidant, analgesic, and antimicrobial. The thiazole scaffold has been detected in more than eighteen FDA-accepted medicines in addition to countless research compounds. A literature review on these themes was undertaken from 2015 to the present. Older publications were not investigated since they had already been peer-reviewed.

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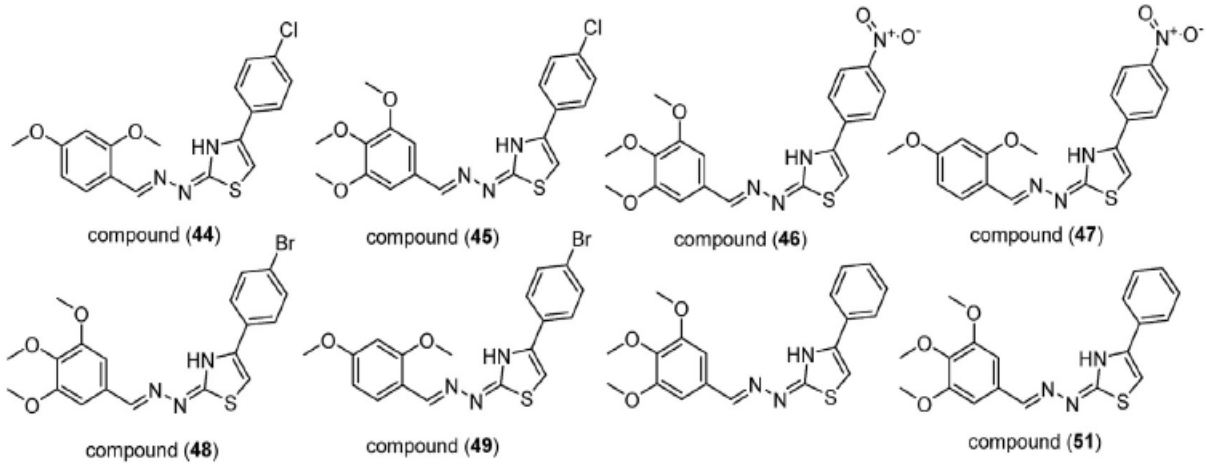
INTRODUCTION

The inclusion of a thiazole ring in the first antibiotics used to treat bacteria (penicillin) was not by chance. There were other marketed drugs having thiazole moieties in certain illnesses. Thiazole derivatives are a diverse family of heterocyclic chemicals with therapeutic effects for a wide range of diseases (Shirai et al., 2013). These compounds exhibit antifungal, antibacterial, non-inflammatory, anesthetic, and anti-cancer (Lino et al., 2018; Sinha et al., 2018; Leoni et al., 2014) capabilities. Many patent applications for antibacterial thiazole compounds have been filed. It has been seen that creating and producing chemical molecules having more than one thiazole loop component improves their medicinal benefits. As a result, various researchers are concerned with in the creation of molecules having multiple thiazole moieties (Althagafi et al., 2019).

Thiazoles are therapeutical compounds that inhibit Schistosoma mansoni (SM) development. Pareira et al., (2019) investigated the effects of eight new aryl-based thiazole compounds on SM. (Figure1). These analogs killed anywhere from 10% to 40% of the SM worms .

Ahmed O. Maslat et al., (2021) synthesised two new thiazole and thiadiazine compounds and examined their antihyperglycemic and antioxidant properties in diabetic mice produced by streptozotocin (STZ). The two drugs effectively lowered hyperglycemia and restored pancreatic insulin production in diabetic rats. Blood triglycerides fell in diabetic mice treated with the two drugs, while pancreatic SOD activity increased.

Alaa M.Alqahtani and colleagues created 10 novel pyridine-linked thiazole hybrids (2021). The cytotoxicity of the synthesised compounds was tested in HepG2 liver cancer cells, 9Hep-2 laryngeal carcinoma cells, PC3 prostate cancer cells, MCF-7 breast cancer cells, and normal fibroblast cells (E138). The anticancer activity of pyridine-thiazole compounds 7 and 10 against MCF-7 and HapG2 cell lines seemed promising.



(Figure 1)

Cristina Nastasa et al., (2015) synthesised a novel family of high-yielding hydrazones by treating 4 – methyl – 2 – (4 – (trifluoro-methyl) phenyl) thiazole – 5 – carbo-hydrazide with different benzaldehyde substituents. To characterise the generated compounds, elemental, physicochemical and spectral data were employed. In an antibacterial screening, Gram (+),

Gram (-), and one fungal strain were employed. The drugs investigated have varied degrees of growth inhibiting activity. The anti - oxidant capabilities of the samples were evaluated using the 2, 2 – Diphenyl – 1 – picrylhydrazide test.

Tatar et al., (2016) developed novel prototypes that include the pharmacophore, thiourea and 1,3,4-thiadiazole into a single molecular backbone. Three chemicals in their collection stood out due to their prospective activity profiles against Mycobacterium tuberculosis strain H37Rv. The MICs of the two most active compounds were 10.96 and 11.48 M, respectively. With a MIC of 17.81 M, the third chemical inhibited M.tuberculosis strain H37Rv. In the vero cell line, according to cytotoxicity tests these three drugs had selectivity ranging from 1.8 to 8.7. To rationalise the biological outcomes of their derivatives, molecular docking experiments with *M Tuberculosis* noyl acyl carrier protein reductase (InhA) were performed, and these compounds had docking values varying from 7.12 to 7.83 kcal/mol.

Thiazoles are important component of medicinal chemistry due to their various biological effects.Hampannavar et al., isolated four novel styryl hydrazine thiazole hybrids as well as their thiosemicarbozone intermediate derivatives. As a result, the anti-TB efficacy of these drugs (1–5) was assessed INH-R1 (Y-155), INH-R2 (ATCC-35822), RIF-R1 (S522L), RIF-R2 (ATCC35828), and FQ-R1 (fluoro-quinolone resistant strain – D94N) are 5 opposing clinical Mtb strains. INH is an abbreviation for isoniazid, RIF is an abbreviation for rifampicin, and FQ is an abbreviation for fluoro-quinolone.

Guzman Alvarez et al., (2015) revealed the synthesis and pharmacological assessment of new amide-containing thiazoles, as well as their in vivo and in vitro, activity against the causative agent of Chagas disease, Trypanosoma cruzi. The thiazole derivative containing lead amide displayed outstanding in vitro activity, no mutagenic or clastogenic effects, and great in vitro selectivity and in vivo tolerance.

Huda R.M.Rashdan et al., (2020) found methyl – 2 – (1-(3-methyl-6-(p-tolyl)imidazo[2,1-b] thiazole – 2 – yl)ethylidene)hydrazine – 1 – carbo dithioate computer molecular docking study was also carried out to determine whether the thiadiazole derivatives might interact with the active area of the target Glypican – 3 protein (GPC – 3). Furthermore, the physiochemical properties of the produced compounds were investigated in order to determine their applicability as potential therapy options for liver cancer.

Seck et al., (2021) investigated the biological activity of thiazoles and observed that compounds containing the thiazole ring, had anticoronavirus activity. SARSCoV 3CLpro (severe acute respiratory syndrome coronavirus protease) inhibitors were shown to be effective using thiazolyl ketone peptidic derivatives, with compound being the most potent (Ki value of 2.20 M and IC50 of 9.5 M). To optimise the chemical structure, they used molecular docking studies using dimeric chymotrypsin-like proteases.

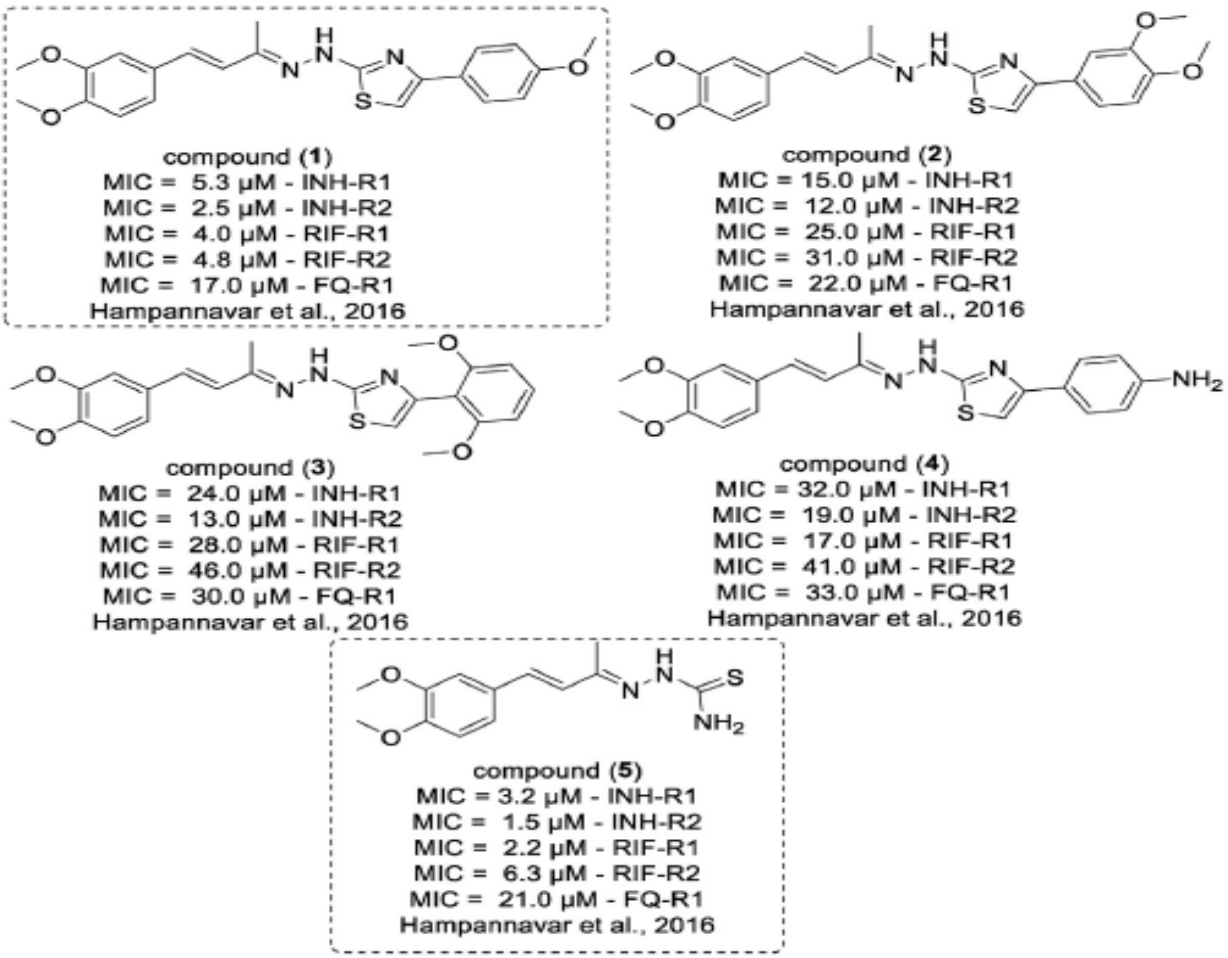


Fig 2 Hampannavar et al. (2016) [24] demonstrated four novel dehydrozingerone styryl hydrazine thiazole hybrids (1-4) and a thiosemicarbazone-intermediary counterpart (5).

Ismail Althagafi et al., (2019) synthesized a novel class of compounds having di, tri, and tetrathiazole moieties and studied its antibacterial and antifungal activities activity against a wide range of bacteria and fungi. These chemicals have been shown

to have antibacterial action. In terms of action, the data showed that di- and trithiazole ring compounds beat traditional antibiotics.

Thiazole and thiazolidinone derivaties, according to Konstantinos Liaras et al., (2018), might be potential candidates for future COX/LOX inhibitor research targeted at generating innovative, more effective, and safer anti-inflammatory medicines.

Linda R. Abdu – Rehem et al., (2021) synthesised and docked novel 2 – amino thiazole compounds before characterising them physically and spectroscopically. The bioactivities of the synthesised derivatives were investigated using Enterobact aerogenes, Escherichia coli, Enterococcus faecalis, Pseudomonas aeruginosa, Staphylococcus aureus, and two fungus strains, Candida albicans and Cryptococcus neoformans var. grubii.

According to Ludek Eyer et al., (2018), nucleoside analogues are the most popular family of related molecule-based antivirals and are currently utilised as the cornerstone of chemotherapy for persistent infections caused by HIV, hepatitis B or C viruses, and herpes viruses. Because of their substantial antiviral activity and favourable pharmacokinetics, several nucleoside equivalents are also effective in treating severe infections evolved by other medically significant RNA and DNA viruses.

Huntington's disease is a neurological disorder for which there is no cure (HD). Luisa Quinti et al. (2016) investigated and found potential thiazole-containing inhibitors of the sirtuin-2 (SIRT2) deacetylase with neuroprotective action in vivo brain slices and Drosophila HD models. Researchers discovered a strong NRF2 activator (MIND4-17) with no SIRT2 inhibiting impact using structure-activity link researches. NRF2 stimulation induced responses in both neuronal and non-neuronal cells, whereas reactive oxygen species and nitrogen intermediates were reduced. These drug-like thiazole-containing molecules might open the way for new therapeutics with synergistic therapeutic advantages in HD and associated diseases.

Yousif and colleagues synthesized functionalized pyrimidine, thioxypyrimidine, iminopyrimidine, and iminopyrimidine derivatives, as well as bicyclic thiazolopyrimidine derivatives (2017). Acetylated thioglycosides were generated after glycosylation of the thiopyrimidine derivative, which were subsequently deacetylated to provide free hydroxythioglycosides. The anticancer activity of the synthesised derivatives was tested in HepG-2 hepatocellular carcinoma, PC-3 human prostate adenocarcinoma, and HCT-116 human colorectal carcinoma cell lines. Three molecules were discovered to be particularly active against PC-3 cancer cells, whereas two molecules were discovered to be more active against the HCT-116 cancerous cell line.

Michelyne Haroun et al., (2021) published their findings on the design, preparation, simulation and hardware antibacterial activity evaluation, and docking research of 5-methylthiazole-based thiazolidinones. All of the compounds were bactericidal in vitro, with many (1, 4, 10, and 13) outperforming E.coli and B.cereus. Compound 12 outperformed reference drugs ampicillin and streptomycin, which were either neutral or simply had a bacteriostatic impact against MRSA.

Morsy et al., (2020) investigated the antibacterial properties of benzothiazole. The inhibitory concentration (MIC; _g/mL) was measured for antibacterial activity against Staphylococcus aureus, Bacillus subtilis, and Escherichia coli, as well as antifungal activity against Candida albicans and Aspergillus niger. Benzothiazole compounds were likely to have MIC values ranging from 25 to 200 g/mL. Some compounds demonstrated significant antibacterial and antifungal activities, whereas rest of the others shown very little activity against all species tested. Several benzothiazole drugs inhibited Candida albicans dimorphism and lowered Escherichia colidihydroorotase activity. In addition, DNA break in Aspergillus niger spores are caused by active benzothiazole compounds. Benzothiazole derivatives' molecular interactions with dihydroorotase resulted in the creation of hydrogen bonds with active site residues. LEU222 or ASN44. Dihydroorotase inhibition may be caused by strong hydrophobic contacts between the bulky thiazole and naphthalene rings at the active site's entrance. These medicines' antibacterial effect may be enhanced by inhibiting dihydroorotase.

Mohamed E. Khalifa et al., (2018) described the manufacturing and clinical assessment of a large number of new benzimidazole compounds and by-product as powerful therapeutic medications for treating microbial infections and inhibiting tumour formation. In vitro experiments on man liver cancer cell lines (HepG2) and man hepatocyte carcinoma cells revealed exceptional antioxidant activity and cytotoxicity at extremely high concentrations.

Omair et al., synthesised new triazoles, tetrazines, and thiadiazoles using commercially available starting materials (2015). The antibacterial activity of the synthesised derivatives was evaluated by spectroscopic and elemental analysis against four distinct species. The compounds demonstrated good anti - bacterial effect when compared to the standard antibiotic. To know more about their function, these compounds were tested for anti-oxidant potential using SOD-like activity, DPPH free radical scavenging activity, ABST, and NO, and the results were promising. Furthermore, even when no external additives were present, these chemicals significantly increased genomic DNA disintegration.

Nivea Pareira de Souza et al. (2017) investigated the potential mechanisms of action of thiazole antibiotics in the treatment of Cryptococcus. Thiazoles were incompatible with parasulphonate phenyl porphyrinato ferrate III as well (FeTPPS). As a result, they discovered that the action of these thiazoles is connected with anti-oxidant system interference.

Guzeldemirci et al., (2017) tested it in mammalian cell cultures against a variety of DNA and RNA viruses. Some of the ingredients have been demonstrated to have potent antiviral properties. The anti—5-methyl-4-thiazolidinone action of the 2009 pandemic virus A/H1N1 Virginia/ATCC3/2009 (cytotoxicity >100 M) was weak but consistent against three influenza A virus strains. In HeLa cells, two compounds had anti-viral EC 50 values of 9 (cytotoxicity 100 M) and 2 M (cytotoxicity 20 M) against vesicular stomatitis virus, respectively. Both anti-HIV medications have been shown to be ineffective.

Pallavi et al., (2019) designed and evaluated a series of methylated benzimidazole nucleosides and screened antiviral activity against maize dwarf mosaic virus. Molecular docking methods were used to explore the binding manner of benzimidazole nucleosides in the active site of maize dwarf mosaic virus. All compounds docked into various locations of the maize dwarf mosaic virus and some exhibited a high docking score, and considered as good antiviral agents.

In their publication, Pervaiz Ali Channar and colleagues address the synthesis of a new family of hydrazine-linked 1, 3-thiazoles (5a-m) (2021). Their motifs' biological importance has been demonstrated by their potent urease inhibitory action. According to an in vitro research, all of the substances are strong urease inhibitors (Allawia et al., 2019).

Radu Tamaian et al., (2015) studied the lipophilicity of 22 thiazolyl – carbonyl thiosemicarbazides and thiazolyl – azole compounds,to find one of the most significant physicochemical properties of bioactive derivatives among them. Principal component analysis (PCA) was used to correlate chromatographically derived lipophilicity characteristics to

estimated log P and log D values, as well as other biological data, to evaluate the anti-inflammatory and anti - oxidant capabilities of the substances investigated.

Azzam et al., (2020) synthesised and evaluated a significant number of novel substituted 2-pyrimidylbenzothiazoles with sulfonamide moieties or amino groups at the pyrimidine ring's C2. The ring system was created in an unusual fashion by employing Michael addition techniques to react guanidine or N-arylsulfonated guanidine with different ylidenebenzothiazole derivatives. The newly synthesised compounds were tested for antiviral activity against HSV-1, CBV4, HAV HM 175, HCVcc genotype 4 viruses, and HAdV7 using a plaque reduction assay. When compared to acyclovir, five of the twenty-one synthesised derivatives reduced viral load by 70-90 percent, with significant IC50, CC50, and SI values. In the case of CBV4, nine derivatives had a decline of more than 50%.When evaluated against HAV, seven of the synthesised compounds yielded comparable results, with just a handful attaining a 50% or more decline against HCVcc genotype 4. Surprisingly, one molecule had wide antiviral activity against all five viruses tested, indicating that it might be useful for antiviral therapy. The five HSV-1 inhibitors also inhibit the Hsp90 protein, with IC50 values ranging from 4.87 to 10.47 g/mL. Surprisingly, when the powerful produced compounds were combined with acyclovir, the IC50 values were lower than when acyclovir was used alone. The strong derivatives were docked into the active site of Hsp90.

From Co (II) and Cu (II) ions, Samira A. Almalki et al., (2021) synthesised two thiazole-based compounds. The thiazole ligand and additional suggested medications (arbidol, avigan, and idoxuridine) used in the COVID-19 pandemic treatment regimen were given pharmacophore profiles. Furthermore, molecular docking was used to collect all interaction information and measure the thiazole molecule's efficacy in interacting with the two COVID-19 proteins in contrast to the other three antivirals. The study found that idoxuridine and thiazole have significant antiviral activities (enol form). This falls short of completely eradicating the pandemic. Despite the fact that arbidol and avigan have no antiviral activity, they were employed in the COVID-19 therapeutic regimen.

Sergi Simakov et al., (2021) used computational and experimental approaches to synthesise and assess the antibacterial effect of 20-nine 4 – (indol – 3 yl) thiazole – two – amines and four-(indol – three yl) thiazole acylamines. In an antibacterial activity research against Gram (+) and Gram (-) bacteria, indole derivatives had MICs ranging from 0.06 to 1.88 milligram/mL, while only six methylindole derivatives exhibited MICs ranging from 0.47 to 1.88 milligram/mL. The strain with the highest resistance discovered as S. aureus, whereas the most vulnerable strain was shown to be S. Typhimurium. Inhibiting CYP51 improves antifungal activity whereas inhibiting E. coli MurB improves antibacterial activity.

Gomha et al., (2017) synthesised a new family of thiazoles with a 1,3,4 – thiadiazole core by treating 2 – (4-methyl -2 phenylthiazole – 5 – carbonyl)- N phenylhydrazinecarbothioamide with the appropriate hydrazonoyl chlorides. Element analysis, spectral analysis, and alternative synthesis were employed to validate the structures of the newly synthesised derivatives. The newly synthesised thiadiazoles were examined for their capacity to inhibit the development of the HepG2 cancer cell line inside liver to determine their cytotoxicity. The relationship between structure and activity was also looked at. Using the MTT assay, all freshly synthesised compounds were tested for anticancer activity against a liver carcinoma cell line (HepG2). When compared to the reference medicine Doxorubicin (IC50= 0.72 M), the compounds had IC50 values of 0.82, 0.9,1.06,1.25,1.29, and 1.88 M.

Stella Casciferro et al., (2020) reviewed the current advancements of Thiazoles, and its benzofused system, and thiazolidinone in addressing antibiotic resistance mechanisms in bacterial cells and communities (biofilms). They also looked at the SAR and therapeutic potential of thiazole and its benzofused derivatives, which are antibiotic resistance mechanism inhibitors used to treat severe drug-resistant diseases. They also looked at all of the microorganisms that were involved in their antibacterial action, as well as the occurrence of spontaneous resistance.

Bhadraiah et al., (2020) tested the antibacterial activity of thizole as 1-(7-methyl-3,5-diphenyl-5H-thiazolo(3,2-) pyrimidine – 6 – yl)ethanone and related compounds against Bacillus cereus (MTCC 8372), Staphylococcus aureus (MTCC 96), and Escherichia coli using agar disc diffusion. The relevant chemicals were diluted in DMF (dimethylformamide) at 50 and 100 g/mL and deposited on the inoculation plates after 2 hours at 4ºC. After 24 hours of incubation at 37°C, the inhibitory zone was measured in cm. Furthermore, using Nystatin as a reference medication, the related compounds were tested in vitro for antifungal efficacy against Aspergillus. Fungi include Aspergillus flavus (MTCC 873), Aspergillus niger (MYCC 28), Fusariumoxysporum (MTCC 284), and Fusariummoniliformes (MTCC 284). (MTCC 156).

REFRENCES

Ahmed, O. M., Bahaa, A., Israa, M. A., Mahmoud, A. H. I., Tashtoush, B. A. (2021) Effect of two novel substituted thiazole and thiadiazine derivatives on experimental type- 1 diabetes mellitus. 1-23

Alaa, M. A, Abrar, A. B., (2021) Synthesis and antiproliferative activity studies of new functionalized pyridine linked thiazole derivatives. Arabian Journal of Chemistry, (14), 102914.

Allawia, H., Al Tarawneh, A. Q., H., Al-limoun, M., Alsharafa, K. (2019). Using 3, 4-dichloro benzoic acid as growth substrate by Brevibacterium spp: Effect of some growth conditions. *Journal of Basic and Applied Research in Biomedicine*, *5*(2), 115-123.

Althagafi, I.I., Abouzied, A.S., Farghaly, T.A., Al-Qurashi, N.T., Alfaifi, M.Y., Shaaban, M.R., Abdel Azizd, M.R.(2019). Novel Nano-sized bis-indoline Derivatives as Antitumor Agents. J. Heterocyclic Chem, **(**56), 391–399.

Álvarez, G., Martínez, J., Varela, J., Birriel, E., Cruces, E., Gabay, M., Leal, S.M., Escobar, P., Aguirre-López, B.;Cabrera, N., et al.(2015). Development of bis-thiazoles as inhibitors of triosephosphate isomerase from Trypanosomacruzi. Identification of new non-mutagenic agents that are active in vivo Panel. Eur. J. Med. Chem, 100,246–

Cau^e, B.S., Fernando, R. P(2016). Thiazole, triazole, thio- and semicarbazone derivatives Promising moieties for drug development for the treatment of tuberculosis European Journal of Medicinal Chemistry Reports, **(**1), 100002.

Cristina, N. T., Mihaela, D., Daniela, B., and Ovidiu, O. (2015) New Hydrazones Bearing Thiazole Scaffold: Synthesis, Characterization, Antimicrobial, and Antioxidant Investigation. Molecules, **(**20), 17325-17338.

Cushman, M.S., Seleem, M., Mayhoub, A.S. (2017) Antimicrobial Substituted Thiazoles and Methods of Use.. United States Patent Patent No.: US 9, 801, 861 B2,.

Esra, T., Sevgi. K., Şükriye, G., Sinem, Ö., Nihan, Ü., Tanıl, K., Erik,D., Graciela, A., Robert, S., Christophe, P., Sadık, K., Fikrettin, Ş., Dharmarajan, S., Perumal, Y., and İlkay, K. (2016) Design, Synthesis, and Molecular Docking Studies of a Conjugated Thiadiazole-Thiourea Scaffold as Anti-tuberculosis Agents. Biol Pharm.Bull, (39), 502-515.

Fairhurst, R.A., Imbach-Weese, P., Gerspacher, M., Caravatti, G., Furet, P., Zoller, T., Christine, F., Haasen, D., Trappe, J., Guthy, D.A., et al. (2015) Identification and optimisation of a 40,5-bisthiazole series of selective phosphatidylinositol-3 kinase alpha inhibitors. Bioorg. Med. Chem. Lett,**(**25), 3569–3574.

G, A. H., Karpoormath,R., Palkar, M.B., Shaikh, M.S., Chandrasekaran, B. (2016) Dehydrozingerone inspired styryl hydrazine thiazole hybrids as promising class of antimycobacterial agents, "Dehydrozingerone inspired styryl hydrazine thiazole hybrids as promising class of antimycobacterial agents", ACS Med. Chem. Lett, (7) 686–691.

Gong, C., Gao, A.H., Zhang, Y.M., Su, M.B., Chen, F., Sheng, L., Zhou, Y.B., Li, J.Y., Li, J., Nan, F.J. (2016) Design,synthesis and biological evaluation of bisthiazole-based trifluoromethyl ketone derivatives as potent HDACinhibitors with improved cellular e_cacy. Eur. J. Med. Chem, **(**112), 81–90.

Guzmán, Á., Javier, V., Eugenia, C., Marcelo, F., Martín, G., Sandra, M. L., Patricia, E., Luis, S., Elva, S., Susana, T., Susy, J. F. T., Gloria, Y., Ninfa, I., Vera, de B., Hugo, C., Mercedes, G. (2015) Identification of a New Amide-Containing Thiazole as a Drug Candidate for Treatment of Chagas' Disease. Antimicrobial Agents and Chemotherapy, (59), 1398-1404.

Huda, R. M. R., Aboubakr, H. A., Ihsan, A. S., Sobhi, M. G., Abdel, M. M. S., and Huda, K. M. (2020) Synthesis, Molecular Docking Screening and Anti-Proliferative Potency Evaluation of Some New Imidazo[2,1-b]Thiazole Linked Thiadiazole Conjugates. Molecules, (25), 1-17.

Insa, S., Filomain, N. (2021) Triazole, imidazole and thiazole-base compounds as potential agents against coronavirus. Result in Chemistry,.100132

Ismail, A., Nashwa, E. and Thoraya, A. F. (2019) New Series of Thiazole Derivatives: Synthesis, Structural Elucidation, Antimicrobial Activity, Molecular Modeling and MOE Docking. Molecules. (24), 1-23.

Kamble, R.D., Meshram, R.J., Hese, S.V., More, R.A., Kamble, S.S., Gacche, R.N., Dawane, B.S. (2016) Synthesis and in silico investigation of thiazoles bearing pyrazoles derivatives as anti-inflammatory agents. Comput. Biol. Chem. (61), 86–96.

Konstantinos, L. I., Maria, F. I.D and Athina, G. (2018) Thiazoles and Thiazolidinones as COX/LOX Inhibitors. Molecules. (23), 1-21.

Leoni, A., Locatelli, A., Morigi, R., Rambaldi, M. Novel (2014) thiazole derivatives: A patent review (2008–2012; Part 1). Expert Opin. Ther. Patents (24), 201–216.

Linda, R., Abdu-Rahem, A.K., Faris, T. A. (2021) Docking and Synthesis of Some 2-Aminothiazole Derivatives as Antimicrobial Agents. Egypt. J. Chem, (64),7269-7276.

Lino, C.I., de Souza, I.G., Borelli, B.M., Matos, T.T.S., Teixeira, I.N.S., Ramos, J.P., de Souza Fagundes, E.M., Fernandes, P.O., Maltarollo, V.G., Johann, S., et al. (2018) Synthesis, molecular modeling studies and evaluation of antifungal activity of a novel series of thiazole derivatives. Eur. J. Med. Chem. **(**151), 248–260.

Lud_ek, E., Radim, N., Erik, de C., Katherine, S.R. and Daniel, R. (2018) Nucleoside analogs as a rich source of antiviral agents active against arthropod-borne flaviviruses. Antiviral Chemistry and Chemotherapy. **(**26), 1-28.

Luisa, Q., Malcolm, C., Se´ bastien, M., Donald, C. L., Leslie, M. T., Aleksey G. K. (2016) SIRT2- and NRF2-Targeting Thiazole-Containing Compound with Therapeutic Activity in Huntington's Disease Models. Cell Chemical Biology, **(**23), 849–861.

Mahmoud, N. M. Y., Wael, A. E., Hebat-Allah, S. A., Hanem, M. A., Nabil, M. Y. (2017) Anticancer Activity of New Substituted Pyrimidines, Their Thioglycosides and Thiazolopyrimidine Derivatives. Journal of Applied Pharmaceutical Science, (11), 021-032.

Michelyne, H., Christophe, T., Aggeliki, K., Anthi, P., Athina, G., Marija, I., Marina, K., Marina, S., Alejandro, C., P˘remysl, M., Nagaraja, S., Katharigatta, N. V., Anroop, B. N., and Heba, S. E. (2021) 5-Benzyliden-2-(5-methylthiazol-2-ylimino)thiazolidin-4-ones as Antimicrobial Agents. Design, Synthesis, Biological Evaluation and Molecular Docking Studies, Antibiotics, **(**10), 1-19.

Mohamed, A. M., Enas, M., Mahmoud, K., Katharigatta, N. V., Anroop, B. N., Khaled, G. and Mahmoud, E. (2020) Screening and Molecular Docking of Novel Benzothiazole Derivatives as Potential Antimicrobial Agents. Antibiotics, **(**9),221.

Mohamed, E. K., Adil, A. G., Fahad, M. K., Tarik, A. A., Abdulraheem, S. A. A. and Mahmoud, A. M. (2018) Synthesis, Antibacterial, and Anti HepG2 Cell Line Human Hepatocyte Carcinoma Activity of Some New Potentially Benzimidazole-5-(Aryldiazenyl)Thiazole Derivatives. Molecules, (23), 1-16.

Mohammed, A. A., Abdelwahed, R. S., and Magdy, M. Y. (2015) Synthesis of Novel Triazoles, Tetrazine, Thiadiazoles and Their Biological Activities. Open Access molecules, **(**20), 2591-2610.

Muhammad, Z.A., Masaret, G.S., Amin, M.M., Abdallah, M.A., Farghaly, T.A. (2017) Anti-inflammatory, analgesic and anti-ulcerogenic activities of novel bis-thiadiazoles, bis-thiazoles and bis-formazanes. Med. Chem. **(**13), 226–238.

Nívea, P., Caroline, M., Cleudiomar, I. L., Paulo, J.S. B., Ludmila, M. B., Daniel, A. S., Renata, B. O., Eleftherios, M. B. B. F., Susana, J. (2017) Heterocycle Thiazole Compounds Exhibit Antifungal Activity through Increase in the Production of Reactive Oxygen Species in the *Cryptococcus neoformans Cryptococcus gattii* Species Complex. Antimicrobial Agents and Chemotherapy.**(**61),2700-2716.

Nuray, U.G., Erkan, P., Lieve, N. (2017) Synthesis and antiviral activity evaluation of new 4-thiazolidinones bearing an imidazo[2,1-b]thiazole moiety. Marmara Pharmaceutical Journal, (22),237-248.

Pallavi, D., Dr. Sarika, A. (2019) Molecular modeling, docking and antiviral studies of benzimidazole nucleoside as possible mdmv inhibitors. International Journal of Research and Analytical Reviews, **(**6), 96-102.

Pember, S.O., Mejia, G.L., Price, T.J., Pasteris, R.J. (2016) Piperidinyl thiazole isoxazolines: A new series of highly potent, slowly reversible FAAH inhibitors with analgesic properties. Bioorg. Med. Chem. Lett. **(**26), 2965–2973.

Pereira, A.S.A., Silveira, G.O., Amaral, M.S. et al. (2019) In vitro activity of aryl-thiazole derivatives against Schistosoma mansoni schistosomula and adult worms. PLoS One (14) 1–23,

Pervaiz, A. C., Aamer, S., Saira, A., Dilawar, H., Markus, K., Syeda, A. S.,Jamshed, I.. (2021) Hydrazine clubbed 1,3-thiazoles as potent urease inhibitors: design, synthesis and molecular docking studies. Molecular Diversity, **(**25), 787–799.

Prajapati, N.P. Patel, K.D., Vekariya, R.H., Patel, H.D., Rajani, D.P. (2019) Thiazole fused thiosemicarbazones: Microwave-assisted synthesis, biological evaluation and molecular docking study. Molecules (24), 1741 21 of 23

Radu, T., Augustin M., Radu S., Ioana I., Anca S.,Ovidiu O., Cristina N., Daniela B. and Brîndu¸sa T. (2015) Study of the Relationships between the Structure, Lipophilicity and Biological Activity of Some Thiazolyl-carbonyl thiosemicarbazides and Thiazolyl-azoles. Molecules, **(**20), 22188-22201.

Rasha, A. A., Rokia, R. O., and Galal, H. E. (2020) Efficient Synthesis and Docking Studies of Novel Benzothiazole-Based Pyrimidinesulfonamide Scaffolds as New Antiviral Agents Hsp90α Inhibitors. ACS Omega, (5),1640-1655.

Reddy, G.M., Garcia, J.R., Reddy, V.H., de Andrade, A.M., Camilo, A., Jr., Ribeiro, R.A.P., de Lazaro, S.R. (2016) Synthesis, antimicrobial activity and advances in structure-activity relationships (SARs) of novel tri-substituted thiazole derivatives. Eur. J.Med. Chem. **(**123), 508–513.

Samira, A. A., Tahani, M. B., Basim, A., Arwa, A., Meshari, M. A., Mohamed, E. K., Nashwa, E. (2021) Synthesis and characterization of new thiazole-based Co(II) and Cu(II) complexes; therapeutic function of thiazole towards COVID-19 in comparing to current antivirals in treatment protocol, Journal of Molecular Structure, 130961.

Santana, T.I., Barbosa, M.O., Gomes, P.A.T.M., Cruz, A.C.N., Silva, T.G., LimaLeite, A.C. (2018) Synthesis, anticancer activity and mechanism of action of new thiazole derivatives. Eur. J. Med. Chem. (144), 874–886.

Sergei, S., Victor, K., Anthi P., Ioannis, N., Athina, G., Marija, I., Marina, K., Jasmina, G., Marina, S., Despoina, T. and Ioannis, S. V. (2021) 4-(Indol-3-yl)thiazole-2-amines and 4-_ndol-3-yl)thiazole Acylamines as Novel Antimicrobial Agents: Synthesis, In Silico and In Vitro Evaluation. Pharmaceuticals, **(**14), 1-29.

Shirai, A., Fumoto, Y., Shouno, T., Maseda, H., Omasa, T. (2013) Synthesis and biological activity of thiazolyl-acetic acid derivatives as possible antimicrobial agents. Biocontrol Sci. (18), 59–73.

Sinha, S., Doble, M., Manju, S.L. (2018) Design, synthesis and identification of novel substituted 2-amino thiazole analogues as potential anti-inflammatory agents targeting 5-lipoxygenase. Eur. J. Med. Chem. **(**158), 34–50.

Sobhi, M. G. Hyam, A. A., Doaa, Z.H H., Aboubakr, H. A., Mohamed, E., Mahmoud, M. E., Huda, K M. (2021) Thiazole-Based Thiosemicarbazones: Synthesis, Cytotoxicity Evaluation and Molecular Docking Study. Drug Design, Development and Therapy, **(**15), 659-677.

Sobhi, M. G., Nabila, A. K., Mohamad, R. A., Yahia, N. M. and Ahmad, M. A. (2017) A facile synthesis and anticancer activity of some novel thiazoles carring ,1,2,4-thiadiazole moiety. Chemistry Central Journal, 0255.

Stella, C., Barbara, P., Daniela, C., Domenico, S., Elisa, G., Girolamo, C., and Patrizia, D. (2020) Thiazoles, Their Benzofused Systems, and Thiazolidinone Derivatives: Versatile and Promising Tools to Combat Antibiotic Resistance. Journal of Medicinal Chemistry, **(**63), 7923 – 7956.

Turan-Zitouni, G., Altıntop, M.D., Özdemir, A., Kaplancıklı, Z.A., Çiftçi, G.A., Temel, H.E. (2016) Synthesis andevaluation of bis-thiazole derivatives as new anticancer agents. Eur. J. Med. Chem. 288–294.

Umesha, K. B., Srikantamurthy, N., Vrushabendra, B., Dileep, C. S., Manasa, C., Chandra., ThejeshKumar, M. P., Shridevi, D. (2020) Thiazolo-Pyrimidine Analogues: Synthesis, Characterization and Docking Studies Guided Antimicrobial Activities. Biointerface Research in Applied Chemistry, **(**11), 9443-9455.

Wang, Y., Wu, C., Zhang, Q., Shan, Y., Gu, W., Wang, S. (2019) Design, synthesis and biological evaluation of novel -pinene-based thiazole derivatives as potential anticancer agents via mitochondrial-mediated apoptosis pathway. Bioorg. Chem. **(**84), 468–477.