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Synthesis and Biological Evaluation of 3 (Benzo[d]Thiazol-2-yl)-2-(Substituted Aryl) Thiazolidin-4-one Derivatives

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Abstract: A series of ten novel 3-(Benzo[d]thiazol-2-yl)-2-((substituted Aryl) thiazolidin-4-one derivatives (3a-3j) have been synthesized by the reaction of (2*E*)-1-[5-(2,6-dimethylphenyl)-1*H*-tetrazol-1-yl]- 3-(substituted aryl) prop-2-en-1-one derivatives (2a-2j) with thioglycolic acid. The compounds (2a-2j) were synthesized by the reaction of 2-amino benzothiazole with different heterocyclic aryl aldehydes. The synthesized compounds were characterized by FT-IR, ^{1}H-NMR, and mass spectrometry. The results of spectroscopic characterization are in agreement with synthesized compounds. The synthesized compounds were evaluated for *in vitro* anti-tubercular activity at a concentration of 0.1 – 100.0 µg/mL by the Microplate Blue Alamar Assay method. Pyrazinamide and streptomycin were used as standard anti-tubercular agents. Two of the compounds (labeled 3c and 3i) showed good anti-tubercular activity when compared with the standards (pyrazinamide and streptomycin), while compounds other compounds (labeled 3a, 3d, 3e, 3h, and 3i) showed comparable activity to pyrazinamide. We reported the successful synthesis of novel benzothiazole clubbed with thiazolidinedione in a single framework, as well as their spectral characterization and *in vitro* anti-tubercular activity.

Keywords: benzothiazole; thiazolidinedione; anti-tubercular activity.

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1. Introduction

Benzothiazole is one of the most important heterocyclic molecules containing nitrogen and sulfur with fused benzene and thiazole rings. Due to their wide biological and pharmacological activity, benzothiazoles are attracting a lot of interest from drug designers [1]. Benzothiazoles also serve as the core nucleus in a variety of drugs, such as viozan (dual D2 dopamine receptor, 2-adrenoceptor agonist), probenazole (herbicide), riluzole (anti-depressant and anxiolytic), Zopolrestat (aldose reductase inhibitor for the treatment of late-stage diabetic complications including neuropathy, etc. [2,3]. Benzothiazole derivatives were synthesized and known to exhibit various biological activities as anticancer [4,5], antibacterial [6,7] and antifungal [8], antimicrobial [9], anti-inflammatory [10] and antidiabetic [11], etc. The benzothiazole nucleus is used to synthesize a wide range of pharmaceutical drugs. There have been several exciting enhancements in the biological activity of benzothiazole derivatives in recent years. These compounds have a significant role in medicinal chemistry because of their

extraordinary pharmacological potential. Diverse modifications to the benzothiazole nucleus have resulted in a wide variety of compounds with various pharmacological characteristics. The synthesis, structures, and biological activities of benzothiazole derivatives have long been a subject of study interest in the field of medicine due to the potential activities demonstrated by these compounds.[12,13].

Tuberculosis (TB) is a chronic infectious illness caused by mycobacteria belonging to the 'tuberculosis complex,' which includes *Mycobacterium tuberculosis, Mycobacterium bovis,* and *Mycobacterium africanum,* among others. *TB* has resurfaced as one of the main causes of mortality globally in the previous decade (nearly 3 million deaths annually). An estimated 8.8 million new cases are diagnosed yearly, resulting in 52,000 fatalities every week, or more than 7,000 per day. These figures, however, only represent a portion of the worldwide TB problem. More than 80% of tuberculosis patients are between the ages of 15 and 49, when they are most economically active, causing significant economic and social concerns[14]. Based on the study of MDR and anti-tubercular activities of 2-substituted benzothiazoles, this confirmed that it is an excellent lead compound for developing novel anti-tubercular agents[15].

In present decades, interest in Benzothiazole chemistry has been increasing rapidly because of its broad range of biological applications, primarily due to the role played by benzothiazole in medicinal chemistry as this moiety offers a more complimentary pharmacokinetic profile and a metabolically stable substitute for carboxylic acid functionalities. The heterocyclic benzothiazole clubbed with thiazolidinedione in a single molecular framework has admirable biological, pharmaceutical, and clinical applications[16-20].

In the current research article, we have reported a synthesis of novel derivatives of 3-(benzo[d]thiazol-2-yl)-2-((substituted aryl) thiazolidine-4-one by microwave-assisted method and conventional method and evaluation of their *in vitro* anti-tubercular activity. The Benzothiazole derivatives were synthesized by conventional as well as Microwave-assisted methods of synthesis. The anti-tubercular activity was evaluated by the Microplate Blue Alamar Assay method, and the results were compared with streptomycin and pyrazinamide [21].

2. Materials and Methods

Melting points were determined with open capillary. FT-IR spectra were recorded on a Jasco model 4010 spectrophotometer, and 1H NMR spectra were recorded in DMSO on a Varian mercury FT-NMR model YH- 300 instruments using TMS as an internal standard. Mass spectra were recorded on GC-MS auto-tune EI instrument.

2.1. Conventional method of synthesis.

2.1.1. General procedure for synthesis of 3-(benzo[d]thiazol-2-yl)-2-((substituted aryl) thiazolidine-4-one:

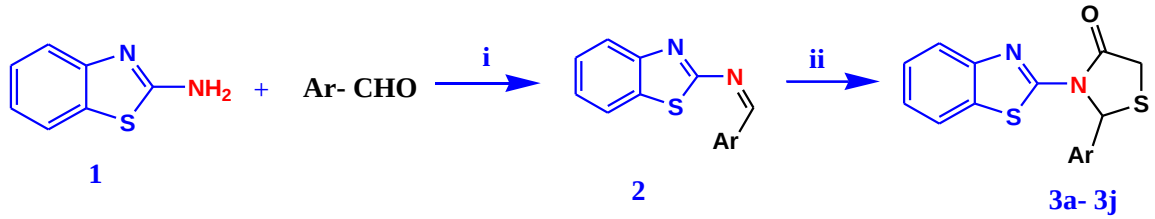
The 2-amino benzothiazole (1) (5 mmol) and substituted aromatic aldehyde (2) (5 mmol) were heated in methanol (15mL) under reflux for 10 min, followed by the addition of a solution of thioglycolic acid forms 3-(benzo[d]thiazol-2-yl)-2-((substituted aryl) thiazolidine-4-one (3 mmol) and. The reaction mixture was heated under reflux for an additional 8-10 h. The progress of the reaction was monitored by TLC (using Hexane: Ethyl acetate 3:2). The mixture was cooled and neutralized with aqueous $NaHCO_3$ (10 %, 30 mL). The formed solid

was filtered off, washed with water three times, and crystallized from ethanol to give crystals of (3a-3j).

2.2. Microwave-assisted synthesis.

2.2.1. General procedure for synthesis of 3-(benzo[d]thiazol-2-yl)-2-((substituted aryl) thiazolidine-4-one.

The 2-amino benzothiazole (1) (5 mmol) and substituted aromatic aldehyde (2) (5 mmol) were heated in methanol (15mL) for 10 min, followed by the addition of a solution of thioglycolic acid forms 3-(benzo[d]thiazol-2-yl)-2-((substituted aryl) thiazolidine-4-one (3 mmol) and. The reaction mixture was irradiated in a microwave oven at level 2 (power 210 watts) for 5 min, respectively. The progress of the reaction was monitored by TLC (using Hexane: Ethyl acetate 3:2). The mixture was cooled and neutralized with aqueous $NaHCO_3$ (10 %, 30 mL). The formed solid was filtered off, washed with water three times, and crystallized from ethanol to give crystals of (3a-3j).



Reagents and conditions:

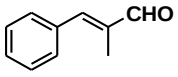
Conventional method: *i) Ar-CHO, MeOH (10 min. reflux),ii) Thioglycolic Acid, MeOH (8 to 10 hr reflux)*

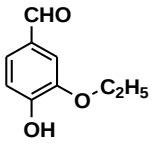
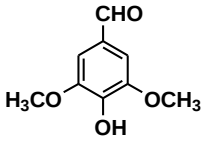
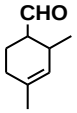
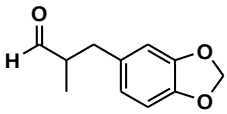
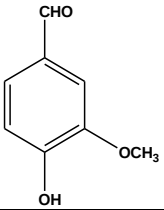
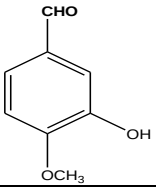
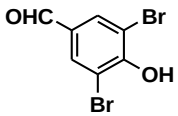
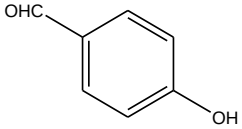
Microwave method: *i) Ar-CHO, MeOH, 5 Min, MW (Power = 2 Level =210 Watt), ii) Thioglycolic Acid, MeOH, 5 Min (Power = 2 Level =210 Watt)*

2.3. Evaluation of anti-tubercular activity.

Tuberculosis disease is caused by *Mycobacterium tuberculosis*, and it mainly causes the lungs and other respiratory organs. In the present study, the antimycobacterial activity of the synthesized compounds (3a-3j) was assessed against *M. tuberculosis* H37Rv (ATCC 2729411) using the Microplate Alamar Blue Assay (MABA) [14,15]. This non-toxic methodology uses thermally stable reagents and shows a good correlation with proportional and BACTEC radiometric methods. The activity was expressed as minimum inhibitory concentration (MIC) in µg/mL. The drug concentrations tested were 0.1 – 100.0 µg/mL. The well's pink tint indicated bacterial growth, while the blue color represented the absence of bacterial growth. As a result, the lowest medication concentration that prevented a color change from blue to pink was known as the MIC (minimal inhibitory concentration). Standards of reference included streptomycin and pyrazinamide.

Table 1. Physical parameters of compound (3a-3j).

Comp no	R	Mole. Formula	MW	% Yield	M.P.^{0}C	R_f.
3a		$C_{19}H_{16}N_2OS_2$	352	65	214	0.62

Comp no	R	Mole. Formula	MW	% Yield	M.P.^{0}C	R_f.
3b		$C_{18}H_{16}N_2O_3S_2$	372	58	180	0.78
3c		$C_{18}H_{16}N_2O_4S_2$	388	62	182	0.68
3d		$C_{16}H_{16}N_2OS_2$	316	72	170	0.72
3e		$C_{18}H_{20}N_2OS_2$	344	70	125	0.65
3f		$C_{20}H_{18}N_2O_3S_2$	398	60	224	0.68
3g		$C_{17}H_{14}N_2O_3S_2$	358	56	174	0.71
3h		$C_{17}H_{14}N_2O_3S_2$	358	55	178	0.68
3i		$C_{16}H_{10}Br_2N_2O_2S_2$	486	52	190	0.58
3j		$C_{16}H_{12}N_2O_2S_2$	328	65	168	0.80

3. Results and Discussion

Table 1 displays the physicochemical characteristics of the synthesized compounds, including melting point. TLC Hexane: Ethyl Acetate 3:2 was used to track the reaction's development. Both conventional and microwave-assisted synthesis techniques produced good yields for the synthesis of all the substances. Regarding yield and time, it is found that the microwave-assisted synthesis technique is superior to the traditional method. The anti-tubercular activity results are listed in Table 2, respectively. In the thiazolidinone series, compounds 3c and 3i showed good anti-tubercular activity compared to both standards pyrazinamide and streptomycin, and compounds 3b, 3c, 3f, 3h, 3k, and 3i showed similar activity compared to standard pyrazinamide. The structure-activity relationship of the compounds shows that the presence of pharmacophoric moieties, such as thiazolidinone moiety, which is attached to benzothiazole in a single molecular framework and different electron-withdrawing substituents, increases anti-tubercular activity. A substituent, such as 4-methoxy, 4-hydroxy group, attached to the phenyl ring and increases the substitution on nitrogen (NH_2 group) with thiazolidinone moiety to give higher activity, perhaps due to an increase in hydrophobicity resulting in better penetration into the *Mtb* cell wall. FT-IR, ^{1}H-NMR, and mass spectra agree with the proposed structures. The compounds' complete spectral data are listed below.

3.1. Spectral data of compound (3a-3j).

3.1.1. 3a : 3-(benzo[d]thiazol-2-yl)-2-((E)-1-phenylprop-1-en-2-yl)thiazolidin-4-one.

IR: 3051(Ar-CH), 1540(C=N), 1442(C=C), 1588-1436 (C-H bend, C=C), 1366 (C-N), 760(C-S),^{1}H NMR: 7.19-8.05 (m, 9H, Ar-H), 1.68 (s, 3H, CH_3), 3.32 (s, 2H, CH_2), 5.25 (s, 1H, Ring-CH), 6.23 (s, 1H, =CH), Mass spectrum (m/z) molecular ion peak at 352.

3.1.2. 3b : 3-(benzo[d]thiazol-2-yl)-2-(3-ethoxy-4-hydroxyphenyl)thiazolidin-4-one.

IR: 3051(Ar-CH), 1540(C=N), 1442(C=C), 1588-1436 (C-H bend, C=C), 1366 (C-N), 760(C-S),^{1}H NMR: 6.55- 8.15 (m, 7H, Ar-H), 1.38 (t, 3H, CH_3), 3.91 (q, 2H, CH_2), 3.32 (s, 2H, CH_2), 5.35 (s, 1H, Ring-CH), 4.9 (s, 1H, -OH),Mass spectrum (m/z) molecular ion peak at 371

3.1.3. 3c : 3-(benzo[d]thiazol-2-yl)-2-(4-hydroxy-3,5-dimethoxyphenyl)thiazolidin-4-one.

IR: 3051(Ar-CH), 1540(C=N), 1442(C=C), 1588-1436 (C-H bend, C=C), 1366 (C-N), 760(C-S),^{1}H NMR: 6.05 - 8.12 (m, 6H, Ar-H), 3.70 (s, 6H, CH_3), 3.32 (s, 2H, CH_2), 5.38 (s, 1H, Ring-CH), 4.96(s, 1H,-OH) ,Mass spectrum (m/z) molecular ion peak at 387.

3.1.4. 3d : 3-(benzo[d]thiazol-2-yl)-2-(cyclohex-3-enyl)thiazolidin-4-one.

IR: 3051(Ar-CH), 1540(C=N), 1442(C=C), 1588-1436 (C-H bend, C=C), 1366 (C-N), 760(C-S),^{1}H NMR: 7.40- 8.12 (m, 4H, Ar-H), 3.32 (s, 2H, CH_2), 4.55 (d, 1H, Ring-CH), 2.46(m, 1H, -CH) 1.45-2.05 (m, 6H, CH_2), 5.55 (q, 1H, =CH), Mass spectrum (m/z) molecular ion peak at 315.

3.1.5. 3e : 3-(benzo[d]thiazol-2-yl)-2-(2,4-dimethylcyclohex-3-enyl)thiazolidin-4-one.

IR: 3051(Ar-CH), 1540(C=N), 1442(C=C), 1588-1436 (C-H bend, C=C), 1366 (C-N), 760(C-S),^{1}H NMR: 7.40- 8.12 (m, 4H, Ar-H), 3.32 (s, 2H, CH_2), 4.55 (d, 1H, Ring-CH), 2.46(m, 1H, -CH), 1.45-2.05 (m, 4H, CH_2), 2.10(q, 1H, -CH-) 1.1 (d, 3H, CH_3), 1.68 (s, 1H, -CH_3), 5.25 (s, 1H, =CH). Mass spectrum (m/z) molecular ion peak at 343.

3.1.6. 3f : 2-(1-(benzo[d][1,3]dioxol-6-yl)propan-2-yl)-3-(benzo[d]thiazol-2-yl)thiazolidin-4-one.

IR: 3051(Ar-CH), 1540(C=N), 1442(C=C), 1588-1436 (C-H bend, C=C), 1366 (C-N), 760(C-S),^{1}H NMR: : 6.50 - 8.12 (m, 7H, Ar-H), 3.32 (s, 2H, CH_2), 4.62(d, 1H, Ring -CH), 2.88(m, 1H, -CH) 1.0(d, 3H, CH_3), 2.55 (d, 2H, CH_2), 5.85 (s, 1H, Ring CH_2) ,Mass spectrum (m/z) molecular ion peak at 397.

3.1.7. 3g : 3-(benzo[d]thiazol-2-yl)-2-(4-hydroxy-3,5-dimethoxyphenyl)thiazolidin-4-one.

IR: 3051(Ar-CH), 1540(C=N), 1442(C=C), 1588-1436 (C-H bend, C=C), 1366 (C-N), 760(C-S),^{1}H NMR: 6.48 - 8.12 (m, 7H, Ar-H), 3.32 (s, 2H, CH_2), 5.88(s, 1H, Ring -CH), 3.7(s, 1H, CH_3), 4.9 (s,1H, -OH),Mass spectrum (m/z) molecular ion peak at 357.

3.1.8. 3h: 3-(benzo[d]thiazol-2-yl)-2-(3-hydroxy-4-methoxyphenyl)thiazolidin-4-one.

IR: 3051(Ar-CH), 1540(C=N), 1442(C=C), 1588-1436 (C-H bend, C=C), 1366 (C-N), 760(C-S),^{1}H NMR: 6.48 - 8.12 (m, 7H, Ar-H), 3.32 (s, 2H, CH_2), 5.88(s, 1H, Ring -CH), 3.7(s, 1H, CH_3), 4.9 (s,1H, -OH), Mass spectrum (m/z) molecular ion peak at 357.

3.1.9. 3i: 3-(benzo[d]thiazol-2-yl)-2-(3,5-dibromo-4-hydroxyphenyl)thiazolidin-4-one.

IR: 3051(Ar-CH), 1540(C=N), 1442(C=C), 1588-1436 (C-H bend, C=C), 1366 (C-N), 760(C-S),^{1}H NMR: 7.05 - 8.15 (m, 6H, Ar-H), 3.32 (s, 2H, CH_2), 5.86 (s, 1H, Ring-CH), 4.95 (s, 1H, -OH),Mass spectrum (m/z) molecular ion peak at 485.

3.1.10. 3j: 3-(benzo[d]thiazol-2-yl)-2-(4-hydroxyphenyl)thiazolidin-4-one.

IR: 3051(Ar-CH), 1540(C=N), 1442(C=C), 1588-1436 (C-H bend, C=C), 1366 (C-N), 760(C-S),^{1}H NMR: 6.60 - 8.15 (m, 8H, Ar-H), 3.32 (s, 2H, CH_2), 5.86 (s, 1H, Ring-CH), 4.9 (s, 1H, -OH),Mass spectrum (m/z) molecular ion peak at 327.

Table 2. The anti-tubercular activity of compounds 3a-3i.

Compound	MIC (µg/ml)
3a	12.50
3b	25
3c	6.25
3d	12.5
3e	12.5
3f	25
3g	12.5
3h	12.5
3i	6.25
3j	12.5
Streptomycin	6.25
Pyrazinamide	3.12

4. Conclusions

The overall outcome of these results reveals that a new series of benzothiazole clubbed with thiazolidinone ring in a single molecular framework is a satisfactory backbone for anti-tubercular activity. The compounds 3c and 3i show good anti-tubercular activity compared to streptomycin and pyrazinamide. While the compounds 3a, 3d, 3e,3g, 3h and 3j shows moderate activity. This preliminary analysis encouraging anti-tubercular results could offer an excellent framework in the field that may lead to the discovery of potent anti-tubercular agents.

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Conflicts of Interest

The authors declare no conflict of interest.

References

1. Froes, T.Q.; Chaves, B.T.; Mendes, M.S.; Ximenes, R.M.; da Silva, I.M.; da Silva, P.B.G.; de Albuquerque, J.F.C.; Castilho, M.S. Synthesis and biological evaluation of thiazolidinedione derivatives with high ligand efficiency to P. aeruginosa PhzS. *Journal of Enzyme Inhibition and Medicinal Chemistry* **2021**, *36*, 1217-1229, https://doi.org/10.1080/14756366.2021.1931165.
2. Zhilitskaya, L.V.; Shainyan, B.A.; Yarosh, N.O. Modern Approaches to the Synthesis and Transformations of Practically Valuable Benzothiazole Derivatives. *Molecules* **2021**, *26*, 2190, https://doi.org/10.3390/molecules26082190.
3. Shainyan, B.A.; Zhilitskaya, L.V.; Yarosh, N.O. Synthetic Approaches to Biologically Active C-2-Substituted Benzothiazoles. *Molecules* **2022**, *27*, 2598, https://doi.org/10.3390/molecules27082598.
4. Stremski, Y.; statkova-abeghe, S.; Kirkova, D.; Angelov, P.; Ivanov, I. Synthesis and structure of new benzothiazole hybrids as potential anticancer agents. *Journal of International Scientific Publications* **2021**, *15*, 173-187.
5. Taghour, M.S.; Elkady, H.; Eldehna, W.M.; El-Deeb, N.M.; Kenawy, A.M.; Elkaeed, E.B.; Alsfouk, A.A.; Alesawy, M.S.; Metwaly, A.M.; Eissa, I.H. Design and synthesis of thiazolidine-2,4-diones hybrids with 1,2-dihydroquinolones and 2-oxindoles as potential VEGFR-2 inhibitors: in-vitro anticancer evaluation and in-silico studies. *Journal of Enzyme Inhibition and Medicinal Chemistry* **2022**, *37*, 1903-1917, https://doi.org/10.1080/14756366.2022.2085693.
6. Haider, K.; Shrivastava, N.; Pathak, A.; Prasad Dewangan, R.; Yahya, S.; Shahar Yar, M. Recent advances and SAR study of 2-substituted benzothiazole scaffold based potent chemotherapeutic agents. *Results in Chemistry* **2022**, *4*, 100258, https://doi.org/10.1016/j.rechem.2021.100258.
7. Haider, K.; Rehman, S.; Pathak, A.; Najmi, A.K.; Yar, M.S. Advances in 2-substituted benzothiazole scaffold-based chemotherapeutic agents. *Arch Pharm (Weinheim)* **2021**, *354*, e2100246, https://doi.org/10.1002/ardp.202100246.
8. Levshin, I.B.; Simonov, A.Y.; Lavrenov, S.N.; Panov, A.A.; Grammatikova, N.E.; Alexandrov, A.A.; Ghazy, E.S.M.O.; Savin, N.A.; Gorelkin, P.V.; Erofeev, A.S.; et al. Antifungal Thiazolidines: Synthesis and Biological Evaluation of Mycosidine Congeners. *Pharmaceuticals* **2022**, *15*, https://doi.org/10.3390/ph15050563.
9. Nasr, A.Z.; Farahat, A.; Zein, M.A.; Abdelrehim, E.-S.M. Synthesis and Antimicrobial Activity of 1,3,4-Oxadiazoline, 1,3-Thiazolidine, and 1,2,4-Triazoline Double-Tailed Acyclo C-Nucleosides. *ACS Omega* **2022**, *7*, 16884-16894, https://doi.org/10.1021/acsomega.1c06339.

10. Dernovšek, J.; Zajec, Ž.; Durcik, M.; Mašič, L.P.; Gobec, M.; Zidar, N.; Tomašič, T. Structure-Activity Relationships of Benzothiazole-Based Hsp90 C-Terminal-Domain Inhibitors. *Pharmaceutics* **2021**, *13*, 1283, https://doi.org/10.3390/pharmaceutics13081283.
11. Kumar, S.; Rathore, D.; Garg, G.; Khatri, K.; Saxena, R.; Sahu, S. SYNTHESIS AND EVALUATION OF SOME BENZOTHIAZOLE DERIVATIVES AS ANTIDIABETIC AGENTS. *International Journal of Pharmacy and Pharmaceutical Sciences* **2017**, *9*, 60, https://doi.org/10.22159/ijpps.2017v9i2.14359.
12. Moodley, R.; Mashaba, C.; Rakodi, G.H.; Ncube, N.B.; Maphoru, M.V.; Balogun, M.O.; Jordan, A.; Warner, D.F.; Khan, R.; Tukulula, M. New Quinoline-Urea-Benzothiazole Hybrids as Promising Anti-tubercular Agents: Synthesis, In Vitro Anti-tubercular Activity, Cytotoxicity Studies, and In Silico ADME Profiling. *Pharmaceuticals (Basel)* **2022**, *15*, 576, https://doi.org/10.3390/ph15050576.
13. Sucheta; Tahlan, S.; Verma, P.K. Biological potential of thiazolidinedione derivatives of synthetic origin. *Chemistry Central Journal* **2017**, *11*, 130, https://doi.org/10.1186/s13065-017-0357-2.
14. Salina Elena, G.; Postiglione, U.; Chiarelli Laurent, R.; Recchia, D.; Záhorszká, M.; Lepioshkin, A.; Monakhova, N.; Pál, A.; Porta, A.; Zanoni, G.; et al. A New Benzothiazolthiazolidine Derivative, 11726172, Is Active In Vitro, In Vivo, and against Nonreplicating Cells of *Mycobacterium tuberculosis*. *mSphere* **2022**, *7*, e00369-00322, https://doi.org/10.1128/msphere.00369-22.
15. Shainyan, B.A.; Zhilitskaya, L.V.; Yarosh, N.O. Synthetic Approaches to Biologically Active C-2-Substituted Benzothiazoles. *Molecules* **2022**, *27*, 2598, https://doi.org/10.3390/molecules27082598.
16. Zhilitskaya, L.V.; Yarosh, N.O. Synthesis of biologically active derivatives of 2-aminobenzothiazole. *Chemistry of Heterocyclic Compounds* **2021**, *57*, 369-373, https://doi.org/10.1007/s10593-021-02914-6.
17. Trotsko, N.; Golus, J.; Kazimierczak, P.; Paneth, A.; Przekora, A.; Ginalska, G.; Wujec, M. Design, synthesis and antimycobacterial activity of thiazolidine-2,4-dione-based thiosemicarbazone derivatives. *Bioorganic Chemistry* **2020**, *97*, 103676, https://doi.org/10.1016/j.bioorg.2020.103676.
18. Aziz, M.N.; Patel, A.; Iskander, A.; Chini, A.; Gout, D.; Mandal, S.S.; Lovely, C.J. One-Pot Synthesis of Novel 2-Imino-5-Arylidine-Thiazolidine Analogues and Evaluation of Their Anti-Proliferative Activity against MCF7 Breast Cancer Cell Line. *Molecules* **2022**, *27*, 841, https://doi.org/10.3390/molecules27030841.
19. Aziz, N.A.A.M.; George, R.F.; El-Adl, K.; Mahmoud, W.R. Design, synthesis, in silico docking, ADMET and anticancer evaluations of thiazolidine-2,4-diones bearing heterocyclic rings as dual VEGFR-2/EGFRT790M tyrosine kinase inhibitors. *RSC Advances* **2022**, *12*, 12913-12931, https://doi.org/10.1039/D2RA01119K.
20. Lončarić, M.; Strelec, I.; Pavić, V.; Rastija, V.; Karnaš, M.; Molnar, M. Green Synthesis of Thiazolidine-2,4-dione Derivatives and Their Lipoxygenase Inhibition Activity With QSAR and Molecular Docking Studies. *Front Chem* **2022**, *10*, 912822, https://doi.org/10.3389/fchem.2022.912822.
21. Abdelrahman, M.A.; Almahli, H.; Al-Warhi, T.; Majrashi, T.A.; Abdel-Aziz, M.M.; Eldehna, W.M.; Said, M.A. Development of Novel Isatin-Tethered Quinolines as Anti-Tubercular Agents against Multi and Extensively Drug-Resistant *Mycobacterium tuberculosis*. *Molecules* **2022**, *27*, 8807, https://doi.org/10.3390/molecules27248807.