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Original Research Article

Synthesis of New Thiazole Derivatives Bearing Thiazolidin-4(5H)-One Structure and Evaluation of Their Antimicrobial Activity

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Conflict of interest: Nil

Abstract:

Antimicrobial resistance was first documented in a study published in the 1940s. Antimicrobial resistance is becoming a global health crisis. Because of this issue, new pharmaceuticals must be created. So, we set out to create some new thiazolidine-4-one derivatives and test their efficacy against bacteria. To get the final products, certain aryl aldehydes were reacted with 2-[(4,5-diphenylthiazol-2-yl)imino]thiazolidin-4-one. Antimicrobial activity of the produced compounds was tested against four species of Candida, five species of gram-negative bacteria, and four species of gram-positive bacteria. At least a 70% yield of the active compounds (4ah) was achieved. Antimicrobial activity was observed in every component. Compound 4f showed the most activity against C. glabrata (ATCC 24433) (MIC: 31.25 g/ml). The most effective compound against all bacterial species, but especially K. pneumoniae (NCTC 9633), was compound 4b (MIC: 62.5 g/ml). In contrast, E. coli (ATCC 25922) was shown to be most susceptible to compound 4c (MIC:31.25g/ml). All eight compounds (4a-4h) shown antibacterial activity against every kind of bacterium and fungal organism tested. The most effective compounds were found to be 4b (2,6-dichlorobenzylidene), 4c (2,6-dihydroxybenzylidene), 4f (1H-pyrrol-2- yl)methylene, 4g (4-triflouromethylbenzylidene), and 4h (2,3,4-trimethoxybenzylidene).

Keywords: Thiazole. Thiazolidin-4-one. Azoles. Antibacterial activity. Anticandidal activity

Introduction

An rising number of multidrug-resistant microbial pathogens and the emergence of additional infectious illnesses have combined to make treatment of infectious diseases a difficult endeavor. Hospitalized patients, AIDS patients who are immune-suppressed, cancer patients receiving chemotherapy, and organ transplant recipients all have a unique set of challenges when it comes to treatment. Emerging resistance to old and antibiotics has produced a major demand for new classes of antimicrobial drugs, despite the enormous number of antibiotics and chemotherapeutics already accessible for medical use. That's why it's crucial to create novel, potent compounds to use as antimicrobials.

The synthetic variety and therapeutic importance of small-ring heterocycles has made them the subject of much study, particularly those containing nitrogen and

sulfur. Thiazoles have been recognized as playing an important role in medicinal chemistry, while being only one of several heterocycles studied as potential therapeutic candidates.

There are many naturally occurring compounds that contain a thiazole ring, including thiamine (vitamin B1), thiamine pyrophosphate (TPP, a coenzyme important in respiration in the Krebs cycle), epothilones, carboxylase, and the large family of macrocyclic thiopeptide antibiotics, including thiostrepton and micrococcin P1. Anticonvulsant, antimicrobial, antituberculous, bacteriostatic activities, antiviral, antimalarial, anticancer, hypertension, inflammation, schizophrenia, HIV infections, hypnotics, and more recently as fibrinojen receptor antagonists with antithrombotic activity and for the treatment of pain. The creation of antihistamine medications often involves thiazole derivatives.

Piperazine rings and amide moieties may be found in the chemical structures of several modern pharmaceuticals. Antifungal, antibacterial, antimalarial, and antipsychotic properties are just a few of the many therapeutic areas that make use of compounds containing piperazines, making them one of the most essential building blocks in modern drug development.

Previous work by our team demonstrated the cholinesterase activity of a few thiazole-piperazine derivatives. After reviewing the aforementioned literature and our own previous results, we were motivated to synthesis a new series of thiazolepiperazine derivatives and test them for antibacterial and anticholinesterase activity in the hopes of discovering novel physiologically active molecules.

Because of their many biological functions, heterocyclic rings have garnered a lot of attention as potential antibacterial agents with novel mechanisms of action. Thiazoles and their derivatives are important scaffolds in medicinal chemistry and are used to create a wide variety of other heterocyclic molecules. The thiazole ring forms the backbone of the chemical structure of numerous pharmaceutically active molecules and natural products, such as thiamin and penicillin G. Compounds in the thiazole family have enhanced lipophilicity and are metabolized by well-established biochemical processes [4]. Thiazoles' remarkable physicochemical properties and promising natural actions are what have sparked such excitement. Thiazole rings are included in many powerful medications, including sulfathiazole (an antibacterial drug) and abafungin (an antifungal drug). Antimicrobial, antitumor, anti-inflammatory, anti-cancer, anti-tubercular antiviral, antioxidant, anti-HIV, anti-hypertensive, antischizophrenic, antiallergic, and analgesic activity have all been demonstrated for thiazole and its derivatives, making them an important pharmacophore. As an aside, it was plain to see that thiazoles have been given a lot of thought due to the fact that they are very potent antibacterial agents.

LITERATURE REVIEW

Colorado-Peralta, et al. (2023), Infections produced by bacteria and fungus have been a persistent problem for humans throughout history. This is why several laboratories have been working on new chemicals to address the issue. New, very efficient antibacterial drugs are developed by modifying existing thiazole and benzothiazole compounds, which have fascinating biological properties. The nitrogen atoms in this heterocycle also make it possible to coordinate with a wide variety of metals, resulting in metal complexes that boost the biological activity of organic ligands utilized in many pharmaceuticals. The thiazole and benzothiazole-based copper complexes that have shown effective antibacterial action against a wide range of bacteria and fungi are summarized in this bibliographical review.

It is cited as: Biernasiuk, A., Kawczyska, M., Berecka-Rycerz, A., et al. (2019), Fifteen new thiazoles having a cyclohexene moiety were synthesized, and their antibacterial activity was studied. Very significant activity against the reference Candida spp. strains was observed for derivatives 3a-3d, 3f, 3n, and 3o (MIC = 0.015-3.91 g/ml). These drugs' efficacy matches or exceeds that of the gold standard, nystatin. Very substantial activity was shown for compounds 3d, 3f, 3n, and 3o against most yeasts isolated from clinical materials (MIC = 0.015-7.81 g/ml). Candida spp. growth was decreased at quantities not shown to be harmful to the mammalian L929 fibroblast in investigations of the most active chemicals. In addition, the lipophilicity of drugs as evaluated by reversed phase thin-layer chromatography was shown to be significantly correlated with their antifungal activity.

Salk, Begüm Nurpelin; Turan-Zitouni, Gülhan; Avuşolu, Betül; and Acar-Evik, Ulviye. (2018), Scientists have been encouraged to look into new compounds with new processes as a result of the emergence of harmful germs resistant to present antimicrobial medications. Herein, we report the synthesis of many novel 2-[2-[4-(ethyl/phenyl)cyclohexylidene]hydrazinyl] The antibacterial effects of 4-(4-substitutedphenyl)thiazole (2a-2o) derivatives were investigated. At room temperature, 4-(ethyl/phenyl)cyclohexane-1-one was reacted with the proper phenacyl bromide in ethanol to provide the corresponding title compounds (2a-2o). FT-IR, 1H-NMR, 13C-NMR, HRMS, and elemental analyses were used to determine the molecular structures of the compounds. The broth microdilution technique was used to evaluate the compounds' antimicrobial properties. Reference medications included chloramphenicol and ketoconazole. 2-[2-(4-phenylcyclohexylidene)hydrazinyl] is one of the chemicals that has been produced.2H-4-phenylthiazole and 2H-2-[2-(4-phenylcyclohexylidene)hydrazinyl]The MIC90 value of 4-(4-chlorophenyl)thiazole (2l) against C. albicans is 1.95, making it almost four times as effective as ketoconazole. The new research helped expand our understanding of the antibacterial properties of molecules within the thiazole class.

Kartsev, V.; Geronikaki, A.; Zubenko, A.; Petrou, A.; Ivanov, M.; Glamoˇclija, J.; Sokovic, M.; Divaeva, L.; Morkovnik, A.; Klimenko, A. (2022), Herein, we detail the strategy, synthesis, and testing of novel heteroaryl (aryl) thiazole derivatives for antibacterial activity. The strategy behind the design was molecular hybridization. The in vitro testing showed that the antibacterial activity of these compounds was modest. Compound 3 showed the highest activity, with MIC and MBC values of 0.23 to 0.7 and 0.47 to 0.94 mg/mL, respectively. Methicillin-resistant Staphylococcus aureus, Pseudomonas aeruginosa, and Escherichia coli were used to investigate the efficacy of three compounds (2, 3, and 4), all of which exhibited more potential than the reference medication ampicillin. The compounds' antifungal activity improved with increasing concentrations (MIC = 0.06-0.47 mg/mL, MFC = 0.11-1.94 mg/mL). Compound 9 showed the highest activity, with MIC values between 0.06 and 0.23 mg/mL and MFC values between 0.11 and 0.47 mg/mL. Docking analyses have shown that the compounds' antibacterial action is mediated by their expected inhibition of the E. coli MurB enzyme, and that their antifungal activity is mediated by their projected inhibition of 14a-lanosterol demethylase.

Thiazole, a five-membered heteroaromatic ring, is a crucial scaffold of many synthetic compounds, as discussed by Borcea, A.-M., Ionut,, I., Cris,an, O., and Oniga, O. (2021). A wide variety of biological activities, including antibacterial, antifungal,

antiviral, antihelmintic, anticancer, and anti-inflammatory properties, are mirrored in the various thiazole-containing compounds that have been authorized for use in clinical settings. In light of its importance in medicinal chemistry, various thiazole and bisthiazole derivatives with biological activity have been described in the scientific literature. In order to encourage more research into the discovery of thiazole-containing drugs, the present review provides an overview of different methods for the synthesis of thiazole and bisthiazole derivatives and describes various compounds bearing a thiazole and bisthiazole moiety possessing antibacterial, antifungal, antiprotozoal, and antitumor activity.

MATERIAL AND METHODS

The Sigma-Aldrich Chemical Company (St. Louis, Missouri, USA) and Merck compounds (Darmstadt, Germany) supplied all of the compounds used in this study. Thin-layer chromatography (TLC) on Silica Gel 60 F254 TLC plates (Merck KGaA, Darmstadt, Germany) was used to observe all reactions. All m.p. values were obtained using an uncorrected MP90 digital melting point apparatus (Mettler Toledo, Ohio, USA). The following spectroscopic devices were used to collect the data: For 1 H-NMR, we used a Bruker DPX 300 FT-NMR spectrometer; for 13C-NMR, we used a Bruker DPX 75 MHz spectrometer (Bruker Bioscience, Billerica, MA, USA); and for M+1 peaks, we used a Shimadzu 8040 LC/MS/MS instrument. (Shimadzu, Tokio, Japan). The Leco 932 CHNS analyzer (Leco, Michigan, USA) was used for the elemental testing.

5-(2,3-Dichlorobenzylidene)-2-[(4,5-diphenylthiazol-2-yl)imino]-1,3-thiazolidin-4-one (4a)

m. p. 296o C, 1 H-NMR (300 MHz, DMSO-d6 , ppm) δ 7.31-7.33 (m, 3H, Ar-H), 7.38-7.40 (m, 5H, Ar-H), 7.47-7.50 (m, 2H, Ar-H), 7.55-7.60 (m, H, Ar-H), 7.70 (s, H, Ar-H), 7.77 (d, J= 7.80 Hz, H, Ar-H), 7.84 (s, H, C=C-H), 12.95 (brs, H, N-H). 13C-NMR (75 MHz, DMSO-d6 , ppm) δ 127.53, 128.27, 128.56, 128.74, 128.88, 129.11, 129.53, 129.85, 132.23 (C=C-H), 166.80 (C=O). For C25H15Cl2 N3 OS2 calculated: Elemental Analysis: C, 59.06%; H, 2.97%; N, 8.26%; found: C, 59.04%; H, 2.95%; N, 8.29%. HRMS (m/z): [M+H] + calculated for C25H15Cl2 N3 OS2 : 508.0106; found: 508.0108.

5-(2,6-Dichlorobenzylidene)-2-[(4,5-diphenylthiazol-2-yl)imino]-1,3-thiazolidin-4-one (4b)

m. p. 257o C, 1 H-NMR (300 MHz, DMSO-d6 , ppm) δ 7.21-7.26 (m, 2H, Ar-H), 7.31-7.38 (m, 8H, ArH), 7.50 (t, J=8.03 Hz, H, Ar-H), 7.62 (d, J=7.88 Hz, 2H, Ar-H), 7.68 (s, H, C=C-H), 12.90 (brs, H, N-H). 13C-NMR (75 MHz, DMSO-d6 , ppm) δ 127.81, 128.52, 128.64, 128.74, 129.02, 129.20, 129.47, 129.81, 131.63, 132.03, 132.19, 133.47, 133.71, 134.42 (C=C-H), 146.38, 155.71, 165.98, 166.22 (C=O). For C25H15Cl2 N3 OS2 calculated: Elemental Analysis: C, 59.06%; H, 2.97%; N, 8.26%; found: C, 59.09%; H, 2.94%; N, 8.28%. HRMS (m/z): [M+H]+ calculated for C25H15Cl2 N3 OS2 : 508.0106; found: 508.0108.

5-(3,4-Dihydroxybenzylidene)-2-[(4,5-diphenylthiazol-2-yl)imino]-1,3-thiazolidin-4-one (4c)

m. p. 237o C, 1 H-NMR (300 MHz, DMSO-d6 , ppm) δ 6.92 (d, J=8.24 Hz, H, Ar-H), 7.03-7.07 (m, H, ArH), 7.14 (s, H, Ar-H), 7.40 (s, 6H, Ar-H), 7.47-7.50 (m, H, Ar-H), 7.58 (s, 3H, Ar-H), 7.95 (s, H, C=C-H), 9.35 (brs, H, O-H), 9.94 (brs, H, O-H), 12.60 (brs, H, N-H). 13C-NMR (75 MHz, DMSO-d6 , ppm) δ 116.60, 117.74, 120.77, 124.26, 125.41, 128.34 and 128.45, 128.77 and 128.83 and 128.88, 129.46 and 129.51, 129.83 and 129.89, 131.93, 132.03, 133.59 (C=C-H), 134.63, 134.78, 146.29 and 146.36, 149.04, 157.27, 162.75, 166.64, 167.61, 174.59 (C=O). For C25H17N3 O3 S2 calculated: Elemental Analysis: C, 63.68%; H, 3.63%; N, 8.91%; found: C,

63.69%; H, 3.60%; N, 8.93%. HRMS (m/z): [M+H] + calculated for C25H17N3 O3 S2 : 472.0784; found: 472.0791.

5-((1H-indol-3-yl)methylene)-2-[(4,5-diphenylthiazol-2-yl)imino]-1,3-thiazolidin-4-one (4d)

m. p. 228o C, 1 H-NMR (300 MHz, DMSO-d6 , ppm) δ 7.20 (d, J=7.47 Hz, H, Ar-H), 7.24-7.26 (m, H, ArH), 7.29-7.31 (m, 3H, Ar-H), 7.41 (s, 5H, Ar-H), 7.48 (d, J=1.62 Hz, H, Ar-H), 7.54 (d, J=7.89 Hz, H, Ar-H), 7.61 (d, J=6.78 Hz, H, Ar-H), 7.77 (d, J=2.71 Hz, H, Ar-H), 7.95 (t, J=3.84 Hz, H, Ar-H), 8.03 (s, H, C=C-H), 12.26 (brs, H, N-H), 12.41 (brs, H, N-H). 13C-NMR (75 MHz, DMSO-d6 , ppm) δ 111.40, 112.93, 117.83, 119.13, 121.52, 123.58, 125.48, 127.01, 128.35 and 128.41, 128.79 and 128.92, 129.47 and 129.51, 129.83 and 129.88, 132.03, 134.78 (C=C-H), 136.76, 146.09, 156.78, 166.84, 167.43, 174.61 (C=O). For C27H18N4 OS2 calculated: Elemental Analysis: C, 67.76%; H, 3.79%; N, 11.71%; found: C, 67.77%; H, 3.76%; N, 11.74%. HRMS (m/z): [M+H] + calculated for C27H18N4 OS2 : 479.0995; found: 479.0998.

2-[(4,5-diphenylthiazol-2-yl)imino]-5-((1-methyl-1H-pyrrol2-yl)methylene)-1,3-thiazolidin-4-one (4e)

m. p. 224 o C, 1 H-NMR (300 MHz, DMSO-d6 , ppm) δ 4.03 (s, 3H, CH3), 7.29-7.32 (m, 4H, Ar-H), 7.37-7.38 (m, 7H, Ar-H), 7.48-7.52 (m, 3H, Ar-H), 12.19 (brs, H, N-H). 13C-NMR (75 MHz, DMSO-d6 , ppm) δ 35.52 (CH3), 128.34, 128.77, 129.46, 129.83, 130.30, 132.04, 134.78, 146.10 (C=C-H), 163.88, 167.24, 174.59 (C=O). For C24H18N4 OS2 calculated: Elemental Analysis: C, 65.14%; H, 4.10%; N, 12.66%; found: C, 65.10%; H, 4.09%; N, 12.68%. HRMS (m/z): [M+H] + calculated for C24H18N4 OS2 : 443.0995; found: 443.0992.

5-((1H-pyrrol-2-yl)methylene)-2-[(4,5-diphenylthiazol-2-yl) imino]-1,3-thiazolidin-4-one (4f)

m. p. 220o C, 1 H-NMR (300 MHz, DMSO-d6 , ppm) δ 7.30 (d, J=1.30 Hz, 3H, Ar-H), 7.37-7.38 (m, 7H, Ar-H), 7.48-7.51 (m, 4H, Ar-H), 12.17 (brs, 2H, N-H). 13C-NMR (75 MHz, DMSO-d6 , ppm) δ 128.35, 128.78, 128.85, 129.47, 129.83, 132.03, 134.78, 146.10 (C=C-H), 163.89, 167.25, 174.59 (C=O). For C23H16N4 OS2 calculated: Elemental Analysis: C, 64.47%; H, 3.76%; N, 13.07%; found: C, 64.50%; H, 3.74%; N, 13.09%. HRMS (m/z): [M+H] + calculated for C23H16 N4 OS2 : 429.0838; found: 429.0832.

2-[(4,5-diphenylthiazol-2-yl)imino]-5-(4-(trifluoromethyl) benzylidene)-1,3-thiazolidin-4-one (4g)

m. p. 120o C, 1 H-NMR (300 MHz, DMSO-d6 , ppm) δ 7.34-7.41 (m, 10H, Ar-H), 7.82 (s, H, C=C-H), 7.86-7.94 (m, 4H, Ar-H), 12.90 (brs, H, N-H). 13C-NMR (75 MHz, DMSO-d6 , ppm) δ 126.50 and 126.54, 128.38, 128.60, 128.78, 128.97, 129.09, 129.54, 129.87, 130.60, 130.99, 131.76, 138.01 (C=C-H), 167.13 (C=O). For C26H16F3 N3 OS2 calculated: Elemental Analysis: C, 61.53%; H, 3.18%; N, 8.28%; found: C, 61.55%; H, 3.20%; N, 8.25%. HRMS (m/z): [M+H]+ calculated for C26H16F3 N3 OS2 : 508.0760; found: 508.0755.

2-[(4,5-diphenylthiazol-2-yl)imino]-5-(2,3,4- trimethoxybenzylidene)-1,3-thiazolidin-4-one (4h)

m. p. 213o C, 1 H-NMR (300 MHz, DMSO-d6 , ppm) δ 3.73 (d, J=2.67 Hz, 3H, O-CH3), 3.79 (d, J=5.02 Hz, 6H, O-CH3), 6.99 (d, J=8.72 Hz, 2H, Ar-H), 7.31-7.38 (m, 9H, Ar-H), 7.48 (s, H, C=C-H), 7.69 (d, J=8.05 Hz, H, ArH), 12.74 (brs, H, N-H). 13C-NMR (75 MHz, DMSO-d6 , ppm) δ 56.40 (O-CH3), 108.22, 128.54, 128.76, 128.94, 129.29, 129.49, 129.80, 131.82, 132.91, 134.77 (C=C-H), 146.75, 153.63, 167.35 (C=O). For C28H23N3 OS2 calculated: Elemental Analysis: C, 63.50%; H, 4.38%; N, 7.93%; found: C, 63.46%; H, 4.40%; N, 7.91. HRMS (m/z): [M+H] +

calculated for C28H23N3 OS2 : 530.1203; found: 530.1204.

RESULTS AND DISCUSSION

Chemistry

In this work, we synthesized eight novel compounds using 2-[(4,5-diphenylthiazol-2-yl)imino]benzo[d]pyrazole [2,3-d]pyrimidine [1,4-d]pyrimidine- a central 1,3-thiazolidin-4-one moiety. There were four stages to the synthesizing process. The ring closure reaction between 2-bromo-1,2-diphenylethan-1-one and thiourea was the initial step. Chloroacetyl chloride was used to acetylate (1), the resulting intermediate. After adding sodium thiocyanate to 2-chloro-N-(4,5-diphenylthiazol-2-yl) acetamide (2), the resulting 2-[(4,5-diphenylthiazol-2-yl)amino] compound was isolated.the compound 1,3-thiazolidin-4-one (3). Last but not least, 5-substituted-2-[(4,5-diphenylthiazol-2-yl)imino]- 1,3-thiazolidin-4-one derivatives (4a-h) were synthesized by reacting compound 3 with aryl aldehyde derivatives, as seen in Figure 1. Analytical and spectral data were collected and used to properly characterize all produced substances.

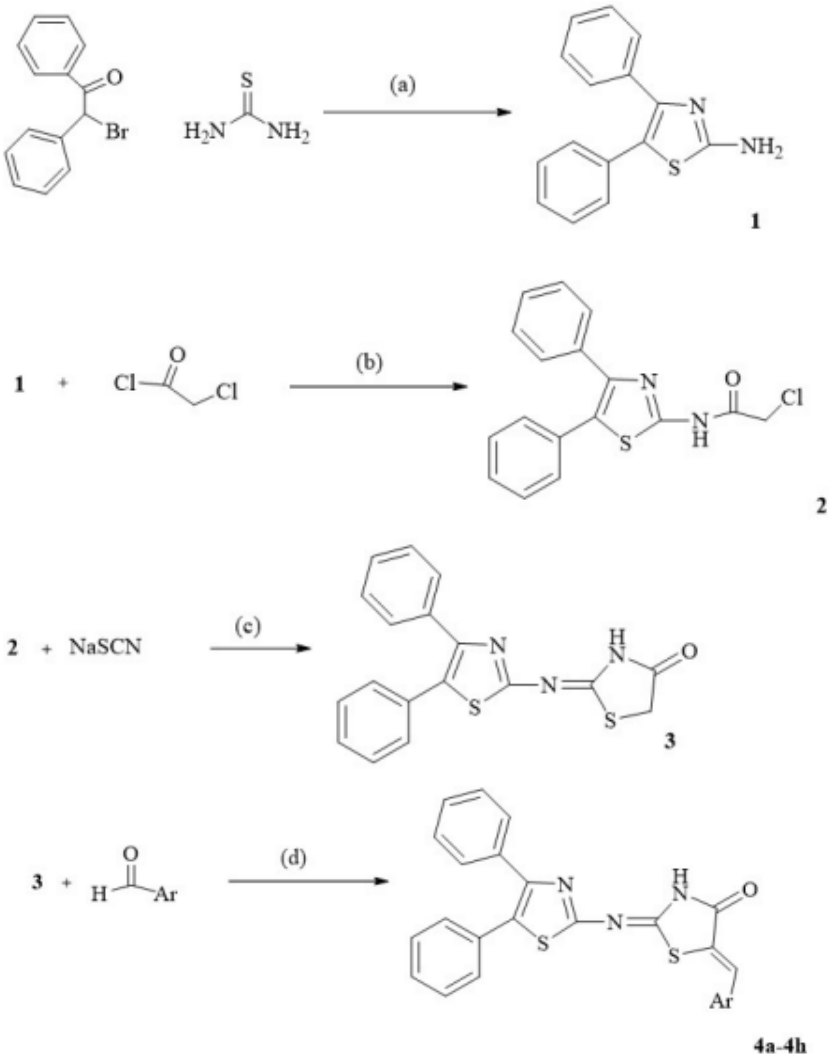
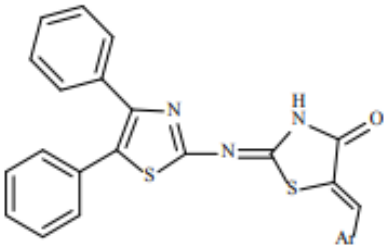
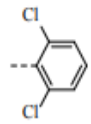
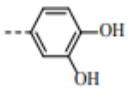
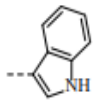


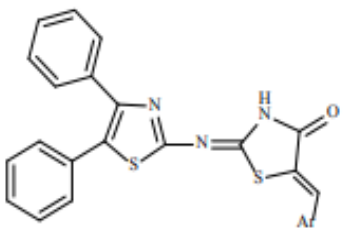
Figure 1: The general reaction diagram of the compounds (4a-4h). Reagents and conditions: (a) EtOH, r.t., 6 h; (b) TEA, THF, ClCOCH2 Cl, 0-5 ºC, then r.t 3 h; (c) EtOH, reflux, 6 h; (d) CH3COOH, NH4 COOCH3 , 6 h, reflux.

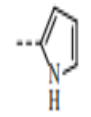
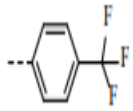
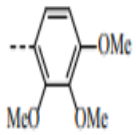
Compound 1 H-NMR spectra exhibited methylene (-C=C-H) proton signals at 7.48-8.03 ppm. The proton of the N-H was denoted by a wide peak at 12.17-12.95 ppm. Due to the aromatic protons, pairs of singlets, doublets, triplets, and/or multiplets appeared around 6.92–7.95 ppm. Compound 13C-NMR spectra showed indications for aromatic carbon (108.22-167.61 ppm) and carbonyl (C=O) carbon (166.22-174.61 ppm). The molecular weights (4a- 4h) of the analyzable compounds agreed with those shown as M+1 peaks in the LC-MS/MS spectra. The computed values of the compounds were consistent with the findings of elemental analysis for C, H, and N. Even though we gave it our best shot, we were unable to determine the isomerism kind that had evolved. The Z isomer is generated in the Knoevenagel reaction if the two structures share a core (Abdelazeem, Salama, Maghrabi, 2015; Momose et al., 1991; Vicini et al., 2008). As a result, there is a good chance that our final compounds will exhibit the Z isomer.

Table 1: Synthesized compounds (4a-4h) and their some physicochemical parameters



	Ar	M. P. (°C)	M. W.	M. F.	Yield (%)	Log P	DL*	V.L.
4a		295-297	508.44	$C_{25}H_{15}Cl_2N_3OS_2$	78	8.05	0.19	2
4b		256-258	508.44	$C_{25}H_{15}Cl_2N_3OS_2$	80	8.05	0.33	2
4c		236-238	471.55	$C_{25}H_{17}N_3O_3S_2$	70	5.83	0.48	1
4d		227-229	478.59	$C_{27}H_{18}N_4OS_2$	78	6.95	-0.91	1
4e		223-224	442.56	$C_{24}H_{18}N_4OS_2$	79	6.02	0.58	1



	Ar	M. P. (°C)	M. W.	M. F.	Yield (%)	Log P	DL*	V.L.
4f		219-221	428.53	$C_{23}H_{16}N_4OS_2$	79	5.95	-0.66	1
4g		119-121	507.55	$C_{26}H_{16}FN_3OS_2$	75	7.69	-0.36	2
4h		212-214	529.63	$C_{28}H_{23}N_3OS_2$	78	6.63	0.30	2

M.P: Melting Point, M.W: Molecular Weight, M.F: Molecular Formula, c Log P: Octanol/water partition coefficient, D.L: Drug-likeness model score, V.L: Violations of Lipinski Rule. For ketoconazole, its Log P value and D.L. score were stated 3.77 and 1.32, respectively. For chloramphenicol, its Log P value and D.L. score were stated 0.73 and 0.63, respectively. Log P was calculated by www.molinspiration.com/cgi-bin/properties (Accessed: December 22, 2017). DL model score was calculated by http://molsoft.com/mprop/software (Accessed: December 22, 2017)

Antimicrobial Activity

The antimicrobial activity of the compounds 4a-4h was investigated by finding MIC values as shown in TABLE 2 and 3.

Table 2: Antifungal activity of the compounds 4a-4h as MIC values (µg/mL)

	4a	4b	4c	4d	4e	4f	4g	4h
A	125	125	125	62.5*	125	125	62.5	62.5
B	62.5	62.5	62.5	62.5	62.5	62.5	62.5	62.5
C	62.5	62.5	62.5	62.5	62.5	31.25*	62.5	62.5
D	125	125	125	125	125	125	62.5*	62.5*
S. D.	<15.625	<15.625	<15.625	<15.625	<15.625	<15.625	<15.625	<15.625

*: Most active compounds. A: C. albicans (ATCC 24433), B: C. krusei (ATCC 6258), C: C. glabrata (ATCC90030), D: C. parapsilopsis (ATCC 22019). S.D: Standard Drug=Ketoconazole.

Table 3: Antibacterial activity of the compounds 4a-4h as MIC values (µg/mL)

	A	B	C	D	E	F	G	H	I
4a	125	125	125	125	125	125	62.5*	125	125
4b	62.5*	62.5	<31.25*	62.5*	62.5*	62.5*	62.5*	62.5*	62.5*
4c	125	<31.25*	125	125	125	125	125	125	62.5*
4d	125	125	125	62.5*	125	125	125	125	125
4e	125	125	125	125	125	125	125	125	125
4f	125	125	125	125	125	125	125	125	125
4g	125	125	125	125	125	125	125	125	125
4h	125	250	62.5	62.5*	62.5*	62.5*	62.5*	125	125
S. D.	7.8125	7.8125	15.625	15.625	7.8125	7.8125	15.625	7.8125	15.625

Scores of 4b and 4c on the DL were found to be comparable to those of gold-standard medications. When comparing the log P values of the synthesized compounds to the standards, however, the values of the most active compounds (4b and 4c) were found to be greater. While a rise in Log P may improve the strength of an effect, it may also reduce the degree of solubility in the solvent used in activity assays. As a consequence, it's possible that the dissolving issue altered the outcome of the experiment.

There was antifungal activity in every chemical. Compound 4f, in particular, showed significant activity against C. glabrata (MIC: 31.25 g/ml). C. albicans (ATCC 24433) was also susceptible to 4d, 4g, and 4h at the same dose (MIC: 62.5 g/ml) and showed antifungal activity. Antifungal activity at the same concentration (MIC: 62.5 g/ml) was revealed for the two most active compounds, 4g and 4h, against all Candida species. C. albicans (ATCC 24433) and C. parapsilopsis (ATCC22019) both showed susceptibility to the other compounds (4a, 4b, 4c, 4d, 4e, and 4f) at the same concentration (MIC: 125.0 g/ml). C. krusei (ATCC 6258) and C. glabrata (ATCC 90030) were both susceptible to the antifungal effects of compounds 4a, 4b, 4c, 4d, and 4e at the same concentration (MIC: 62.5 g/ml).

We concluded that 4f was the most effective chemical in our study of its antifungal properties. It was hypothesized that methylene substitution for (1H-pyrrol-2-yl) at position 5 of thiazolidinone may be to blame. The nucleus of 2-substituted-1H-pyrrole provides an explanation for this, since it has been shown to have antifungal action (Bhardwaj et al., 2015).

In addition, each molecule showed antimicrobial properties. chemical 4b was the most effective chemical overall, killing all tested strains of bacteria with a MIC of 62.5 g/ml. Compound 4b was shown to be the most active against K. pneumoniae (NCTC 9633) while compound 4c was found to be the most active against E. coli (ATCC 25922), both with MICs of 31.25 g/ml. E. coli (ATCC 35218) and B. subtilis (NRRL NRS 744) were both twice as susceptible to compound 4b (MIC: 62.5 g/ml). For Y. enterocolitica (Y53), the most effective compounds were 4b, 4d, and 4h (MICs: 62.5 g/ml). Compounds 4b and 4h were also more effective than the control group against S. typhimurium (ATCC 13311) and S. aureus (ATCC 25923) (MIC: 62.5 g/ml). In addition, L. monocytogenes (ATCC 19111) was shown to be more susceptible to compounds 4a, 4b, and 4h

(MICs: 62.5 g/ml). Similar claims of superiority against E. faecalis (ATCC 29212) were made for strains 4b and 4c (MIC: 62.5 g/ml).

Small groups, such the oxo substitution in the fourth position of thiazole4(5H)-one, may explain the antibacterial activity seen across the board. The addition of 2,6-dichlorobenzylidene (compound 4b) to the 5-position of thiazole-4(5H)-one enhanced its antibacterial activity, as shown by these findings. The great solubility of these compounds in organic phase may be due, at least in part, to their high log P values (Lipinski et al., 1997). Possible contributing factor: the influence of fifth-position thiazole-nucleus replacement in the aforementioned investigation (Bondock, Naser, Ammar, 2013). Substitution types and their relative locations on the benzene ring are known to have significant effects. In this case, it was found that the antibacterial activity enhanced when electron-withdrawing groups like chloride were present at the ortho and meta locations of the benzene ring. These factors could explain why compound 4b was more potent than the others.

Conclusion

Our results show that new 5-substituted-2-[(4,5-diphenylthiazol-2-yl)imino] compounds may be produced.In this research, we tested the antibacterial efficacy of four fungus and nine bacterial species against 1,3-thiazolidin-4-one derivatives (4a-4h). All eight compounds (4a-4h) shown antibacterial activity against every kind of bacterium and fungal organism tested. For combating Candida species, 4g and 4h were the most effective chemicals. K. pneumoniae (NCTC 9633) is the focus of Compound 4b's intense attention, despite the fact that it was equally effective against other bacterial species. In addition, E. coli (ATCC 25922) was most susceptible to compound 4c.

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