

ANTI-MICROBIAL EVALUATION OF NEW THIAZOLO PYRIMIDINE DERIVATIVES

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Abstract

Twelve new heterocyclic compounds containing thiazolo pyrimidine moiety were thus synthesized.. Compound **2** was synthesized by reaction of α -amino naphthol **1** with potassium isothiocyanate. Reaction of compound **2** with sodium nitrite and hydrochloric acid afforded the corresponding diazonium salt **3**, which converted to 2-hydrazino thiazolo derivatives **4**. Compound **2** carried out to synthesize imidazolo thiazolo derivative **5**, **6** and thiazolo pyrimidino derivative **7**, **8** and **9** respectively. Compound **4** was carried out to synthesize of compound **10**. Compound **10** was carried out to synthesize of triazolo thiazolo and thiadiazolo derivatives **11** and **12** respectively. The structures of all newly synthesized compounds were elucidated by elemental analysis, IR, ¹H-NMR and mass spectral data. The assignments of the new products were tested for Anti-microbial activities. Results are suggesting thiazolo pyrimidine derivatives emerge as valuable compounds with great potential to be used as antibacterial and antifungal agents, and as promising candidates for further efficiency evaluation. The detailed synthesis, spectroscopic data and Anti-microbial activities are reported.

Keywords: Naphthalino, Thiazolo, pyrimidine Derivatives, Anti-microbial, Pharmacological Activity

Introduction

The pyrimidine nucleus is present in a wide range of bioactive natural products. In addition, the pharmacological and biological activities of

pyrimidine derivatives are well documented (Grover et al., 1995; Haggarty et al., 2000; Kappe, 2000; Numazi et al., 2001; Kheder et al., 2008). Pyrimidine derivatives have been previously reported to be platelet aggregation inhibitors, antagonists, anti-coceptive and anti-parkinsonism (Nagawadeet al., 2005; Butnariu et al., 2009; **Guan et al.**, 2010; Mojahidi et al., 2010). Also, hetero cyclic compounds exhibited anthelmintic, anti HIV activity and hypoglycemic activity (Rao et al., 2004). Pyrimidine derivatives were found to possess a variety of pronounced activities such as anti-microbial, analgesic (Fayed et al., 2009; Bahashwan, 2011), antimicrobial (Mosharef et al., 2006; Rashad(i) et al., 2010), anti-avian influenza virus (H5N1) (Rashad (ii) et al., 2010), against herpes simplex virus type-1 (HSV-1) and hepatitis-A virus (HAV), serotonin 5-HT₆ receptor antagonist (Ramakrishna et al., 2011), Antiarrhythmic (Abdel-hafez et al., 2009). Thiazolopyrimidines have hypoglycemic, hypolipidemic, antidiabetic and antileishmanial activities (Lee et al., 2005). Pyrimidine derivatives have biological activities ranging from kinase inhibitors, treatment of disease states associated with angiogenesis [plated derived growth factor, PDGFr, fibroblast growth factor, FGFr, and epidermal growth factor, (EGFr) (Boschelli et al., 1998). The analogous mitogen-activated protein (CSBP/P38) kinase inhibitor, telomerase inhibitor, treatment of arthritis, adult respiratory distress syndrome, chronic obstructive pulmonary disease, or Alzheimer's disease (Boehm et al., 2003). Arylazopyrimidine derivatives showed antitumor activity and anticancer activity (Buddh et al., 2011). In view of these observations and as continuation of our previous works in heterocyclic chemistry, we have herein synthesized some new thiazolopyrimidine, and tested their anti-microbial activities in comparison to Tetracycline and Ketoconazole were used as standard drugs.

Materials and Methods

Chemistry

Melting points were determined on open glass capillaries using an Electro thermal IA 9000 SERIES digital melting point apparatus (Electro thermal, Essex, U.K.) and are uncorrected. Elemental analyses were performed with all final compounds on Elementar, Vario EL, Micro analytical Unit, National Research Centre, Cairo Egypt and were found within ~ 0.4% of the theoretical values. Analytical data were obtained from the Micro analytical Unit, Cairo University, Egypt. The IR spectra (KBr) were recorded on a FT IR-8201 PC spectrophotometer .The ¹H-NMR spectra was measured with Jeol FTGNM-EX 270, 270 MHz instrument in DMSO-d₆ and the chemical shifts were recorded in (δ, ppm) relative to TMS. The Mass spectra were run at 70 eV with a Finnigan SSQ 7000 spectrometer using EI and the values of m/z are indicated in Dalton. TLC (Silica gel,

aluminum sheets 60F₂₅₄, Merck, Darmstadt, Germany) followed the reactions.

2-Amino naphthalino [1,2-d]thiazole (2)

A mixture of compound **1** (0.01 mol) and KSCN (0.01 mol) in acetic acid (50 ml) was placed in freezing mixture and stirred mechanically with addition of Br₂ (0.2mol) for 2hrs., at 0-10⁰C. The reaction mixture was poured onto ice-water, the formed solid product was collected by filtration, washed with water, dried and crystallized from ethanol to give compound **2** as green powder. Yield 68%; mp 285°C; IR (KBr, cm⁻¹): 3285 (NH₂); ¹H-NMR (DMSO-d₆): δ: 6.14 (s, 2H, NH₂, exchangeable with D₂O), 7.12-7.38(m, 6H, ArH) ppm; MS m/z (%) 200(M⁺, 23) corresponding to the molecular formula C₁₁H₈N₂S and at 184 (100, base peak).

2-Diazo naphthalino [1,2-d]thiazole (3)

A stirred solution of compound **2** (0.01 mol) in 35% HCL (10ml) was diazotized at 0-5 ⁰C by a solution of 30% aqueous NaNO₂. Then, the solution poured onto ice water and the solid product was crystallized from ethanol to give compound **3** as yellow powder. Yield 67%; mp 248 °C; IR (KBr, cm⁻¹): 1615-1430(C=N, C=C, Ar); ¹H-NMR (DMSO-d₆): δ: 6.92-7.41(m, 6H, Ar-H) ppm; MS m/z (%): 212(M⁺, 38) corresponding to the molecular formula C₁₁H₆N₃S and at 126(100, base peak).

2-Hydrazino naphthalino [1,2-d]thiazole (4)

A mixture of diazonium salt **3** (0.01 mol) and stannous chloride (0.01 mol) in concentrated hydrochloric acid (40 ml) was stirred over night at room temperature. After cooling (-10⁰C), the obtained solid was filtered off, washed with water, dried, and crystallized from the ethanol to give compound **4** as brown powder. Yield 79%; mp 262°C; IR (KBr, cm⁻¹): 3340-3280 (NH, NH₂); ¹H-NMR (DMSO-d₆): δ: 5.67 (s, 1H, NH, exchangeable with D₂O), 7.12-7.65 (m, 6H, Ar-H), 10.31 (b, 2H, NH₂, exchangeable with D₂O) ppm; MS m/z (%): 215 (M⁺, 21) corresponding to the molecular formula C₁₁H₉N₃S and at 132 (100, base peak).

4-Oxo-3H-imidazolo[3,2-b]naphthalino [1,2-d] thiazole (5)

A mixture of compound **2** (0.1 mol) and ethyl chloroacetate (0.1 mol) in poly phosphoric acid (30 ml) was refluxed for 3hrs. The reaction mixture was poured into water, neutralized with sodium carbonate the separated solid was collected and crystallized from ethanol to give compound **5** as reddish brown. Yield 71%; mp 300°C; IR (KBr, cm⁻¹): 1685(C=O amid); ¹H-NMR (DMSO-d₆): δ: 6.15(s, 2H, CH₂), 6.89-7.34(m, 6H, ArH) ppm; MS m/z (%): 240

(M^+ ,19) corresponding to the molecular formula $C_{13}H_8N_2SO$ and at 158 (100, base peak).

4-(4-chloro phenyl) imidazolo[3,2-b]naphthalino [1,2-d] thiazole (6)

A mixture of compound 2 (0.1 mol) and phenacyl bromide (0.1 mol) in glacial acetic acid (30 ml), in the presence of few drops tri ethylamine, was refluxed for 3h. The reaction mixture was poured into water, the separated solid was collected and crystallized from ethanol to give compound 6 as brown. Yield 59%; mp over 300 °C; IR (KBr, cm^{-1}): 1620-1435 (C=N, C=C, Ar); 1H -NMR (111 (DMSO- d_6) δ : 6.92-7.64 (m, 11H, ArH)ppm; MS m/z (%): 334 (M^+ ,31) corresponding to the molecular formula $C_{19}H_{11}N_2SCl$ and at 183 (100, base peak).

3,5-Dioxo-4H-pyrimidino [3,2-b]naphthalino [1,2-d] thiazole (7)

A mixture of compound 2 (0.1 mol) and diethyl malonate (0.1 mol) in glacial acetic acid (30 ml), in the presence of few drops tri ethyl amine, was refluxed for 3hrs. The reaction mixture was poured into water, the separated solid was collected and crystallized from ethanol to give compound 7 as green. Yield 64%; mp 297 °C; IR (KBr, cm^{-1}): 1690(C=O amid); 1715(C=O amid); 1H -NMR (DMSO- d_6) δ : 7.14-7.52(m, 6H, ArH)ppm; MS m/z(%): 268(M^+ ,31) corresponding to the molecular formula $C_{14}H_8N_2SO_2$ and at 172(100, base peak).

Synthesis of pyrimidino thiazole derivatives 8 and 9

A solution of compound 2 (0.01mol) in DMF (20ml) was added benzyldine ethyl cyano acetate and benzyldine malononitrile respectively (0.01 mol) and piperidine (2drops) refluxed 3hrs. Then, the solvent was evaporated under reduced pressure and the remaining product was titrated with water and acidified with concentrated HCL. After filtration the separated solid was collected and crystallized from proper solvent to give compounds 8 and 9 respectively.

3-Amino-4-ethoxy carbonyl – 5 - (4-chloro phenyl) pyrimidine [3,2 - b] naphthalino [1,2-d] thiazole (8)

Yellow powder(62%),mp 225°C (EtOH/DMF). IR (KBr, cm^{-1}): 3270 (NH_2), 1730(C=O ester); 1H -NMR (DMSO- d_6) δ : 2.14 (t, 3H, CH_3), 3.28 (q, 2H, CH_2), 6.84-7.25 (m, 6H, ArH), 7.54-7.87 (m, 5H, ArH), 10.31 (br, 2H, NH_2 exchangeable with D_2O) ppm; MS m/z (%): 436 (M^+ , 42) corresponding to the molecular formula $C_{23}H_{18}N_3SO_2CL$ and at 235 (100, base peak).

3-Amino-4-cyano – 5 - (4 - chloro phenyl) pyrimidine [3,2-b] naphthalino [1,2-d] thiazole (9)

Brown powder (57%); mp over 300°C (benzene). IR (KBr, cm⁻¹): 3305 (NH₂), 2218 (CN); ¹H-NMR (DMSO-d₆) δ: 7.15-7.36 (m, 6H, ArH), 7.41-7.82 (m, 5H, ArH), 10.43 (br, 2H, NH₂ exchangeable with D₂O) ppm; MS m/z (%): 389 (M⁺, 36) corresponding to the molecular formula C₂₁H₁₃N₄SCL and at 198 (100, base peak).

N"[naphthalino [1,2-d] thiazol-2-yl]-N-(4-chloro phenyl) thio semicarbazide (10)

A mixture of compound **4** (0.1 mol) and 4-chloro phenyl thiocyanate (0.1 mol) in glacial acetic acid (40 ml), was placed in freezing mixture and stirred mechanically for 3 hrs. at 0-10°C. The reaction mixture was poured onto ice-water, the formed solid product was collected by filtration, washed with water, dried and crystallized from ethanol to give compound **10** as yellow powder. Yield 76%; mp 246°C; IR (KBr, cm⁻¹): 3197-3262 (3NH), 1610-1438 (C=N, C=C, Ar); MS m/z (%) 350 (M⁺, 48) corresponding to the molecular formula C₁₈H₁₄N₄S₂ and at 184 (100, base peak).

Synthesis of thiazolo derivatives 11 and 12

A mixture of compound **10** (0.01 mol) and phenacyl bromide and chloro acetic acid respectively (0.01 mol) in ethanol (30 ml) was refluxed for 3 hrs. The reaction mixture was poured into water, the separated solid was collected and crystallized from proper solvent to give compounds **11** and **12** respectively.

2- [2-hydrazino -3, 4 - di (4 - chlorophenyl) - 4, 5 - dihydro thiazol-2-yl] naphthalino [1,2-d] thiazole (11)

Yellow powder (59%); mp over 300°C (EtOH). IR (KBr, cm⁻¹): 3218 (NH), 1617-1442 (C=N, C=C, Ar); ¹H-NMR (DMSO-d₆) δ: 6.32 (s, 2H, CH₂), 6.81-7.37 (m, 6H, ArH), 7.42-7.89 (m, 9H, ArH), 11.14 (s, 1H, NH, exchangeable with D₂O) ppm; MS m/z (%): 521 (M⁺, 41) corresponding to the molecular formula C₂₃H₁₈N₃SOCL and at 158 (100, base peak).

2-[2-hydrazino-3-(4-chlorophenyl)-3H-4-oxo thiazol-2-yl] naphthalino [1,2-d] thiazole (12)

Brown powder (64%); mp 210°C (MeOH). IR (KBr, cm⁻¹): 3265 (NH), 1695 (C=O amide); ¹H-NMR (DMSO-d₆) δ: 6.12 (s, 2H, CH₂), 6.79-7.28 (m, 6H, ArH), 7.32-7.64 (m, 4H, ArH), 10.43 (br, 1H, NH, exchangeable with D₂O) ppm; MS m/z (%): 381 (M⁺, 39) corresponding to the molecular formula C₁₉H₁₃N₄SOCL and at 216 (100, base peak).

Anti-Microbial Activity

The newly tested compounds were evaluated *in vitro* for their antimicrobial activities. The antimicrobial activities are carried out against three bacterial strains *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli* and three fungal strains *Aspergillus fumigates*, *Aspergillus niger* and *Alternaria alternata* employing the nutrient agar disc diffusion method (Arthington et al. 2000) at 100 µg/ ml concentration. Dimethyl sulphoxide (DMSO) was used as blank and it exhibited no activity against any of the used organisms. The antimicrobial activity was determined by measuring of the inhibition zone (Table 1), after 16 -20 hrs. of incubation at 37 °C for bacterial strains and 3-4 days at 37 °C for fungal strains. Tetracycline and Ketoconazole were used as standard drugs bacterial and fungal strains, respectively at 30 µg/ ml concentration.

The Minimum Inhibitory Concentration (MIC)

A current definition of the minimum inhibitory concentration MIC is "the lowest concentration which resulted in maintenance or reduction of inoculums viability". The determination of the MIC involves a semi-quantitative test procedure which gives an approximation to the least concentration of antimicrobial agent needed to prevent microbial growth. The method displays tubes of growth broth containing a test level of preservatives, into which inoculums of microbes was added. The end result of the test was the minimum concentration of antimicrobial. The serial dilution technique (Mostahar et al. 2006) was applied for the determination of MIC of the tested compounds 1-6 against two species of bacterial strains (*S. aureus* and *E. coli*) and two species of fungal strains (*A. niger* and *A. alternata*). Dilution series were set up with 6.25, 12.5, 25, 50 and 100 µg/ ml of nutrient broth medium to each tube , 100 µl of standardized suspension of the test microbes (10⁷ cells/ ml)were added and incubated at 37 °C for 24 hrs. (Table 2).

Cytotoxicity Bioassay

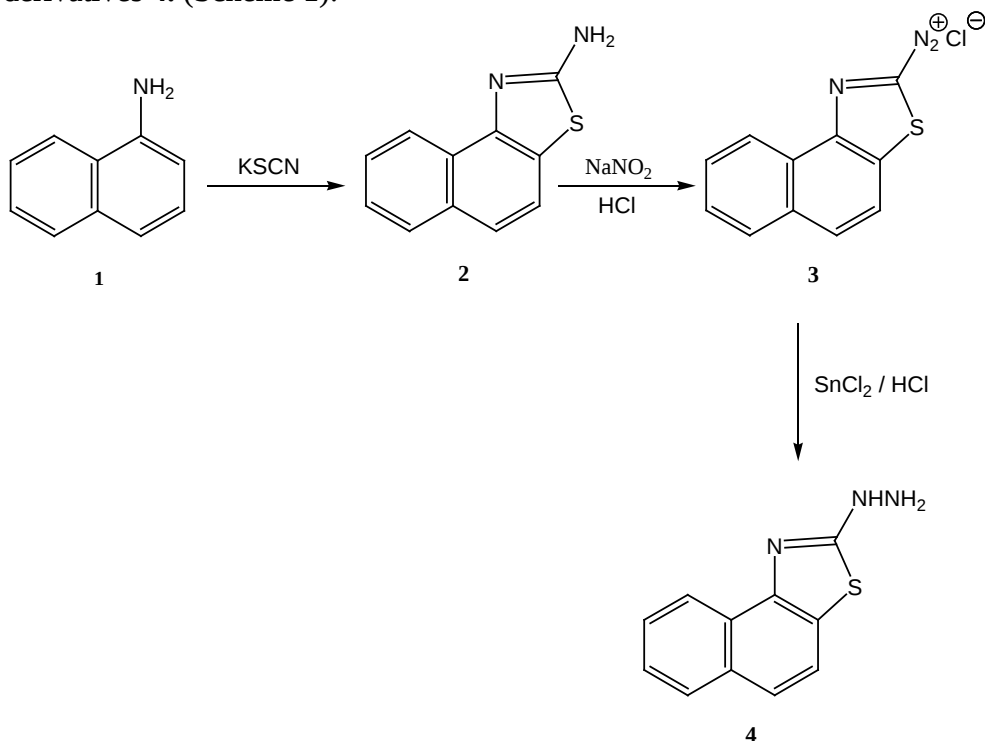
Brine Shrimp lethality bioassay (Mayer et al. 1982 & Jaki et al. 1999) is recent development in the assay which indicates cytotoxicity as well as a wide range of pharmacological activities (e.g. antimicrobial, anticancer, antiviral, insecticidal, pesticidal, AIDS, etc). In this method, the eggs of the brine shrimp, *Artemia salina* leach, were hatched for 48 hrs., to mice shrimp, 38 gm of sea salt was weighed , dissolved in one liter of distilled water, filtered off and was kept in a small tank. The eggs were then added to the divided tank. Constant oxygen supply was provided and temperature 37°C was maintained for 48 hrs. to hatch and mice the shrimp called as nauplii (Larvae). The solutions of compounds 1-6 were prepared by dissolving 10

mg of each compound in 2 ml of DMSO. From this stock, a series of solution 5, 10, 20, 40 and 80 $\mu\text{g/ml}$ were transferred to fifteen vials (three for each dilutions were used for each test sample and LC_{50} is the mean of three values) and one vial was kept as control having 2 ml of DMSO. Then about 10 brine shrimp nauplii were applied to each of all experimental vials and control vial. The number of the nauplii that died after 24 hrs. was counted. The resulting data were transformed to the probit analysis for the determination of LC_{50} values for the five tested compounds (Table 3).

Results and Discussion

Chemistry

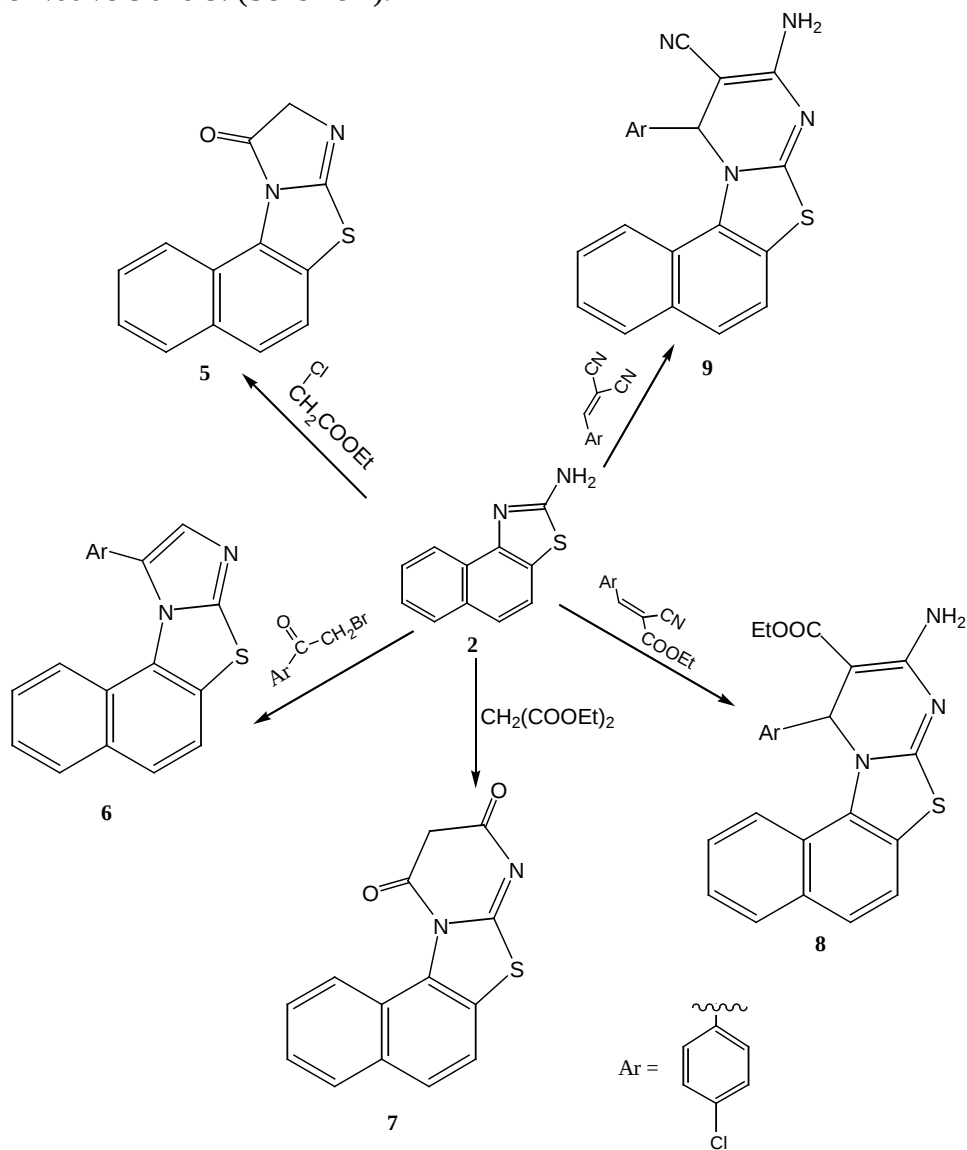
In previous work we have reported the synthesis of thiazolo derivatives used α -amino naphthol **1**. The reaction of compound **1** with KSCN afforded 2-amino thiazolo derivatives **2**. The reaction of compound **2** with sodium nitrite and hydrochloric acid afforded the corresponding diazonium salt **3**, which converted to starting material 2-hydrazino thiazolo derivatives **4**. (Scheme 1).



Scheme 1: Synthetic route of compounds **2** - **4**

The reaction of hydrazino thiazolo derivatives **4** with ethyl chloro acetate and phenacyl bromide respectively in the presence of ethanol afforded the corresponding imidazolo thiazolo derivative **5** and **6**

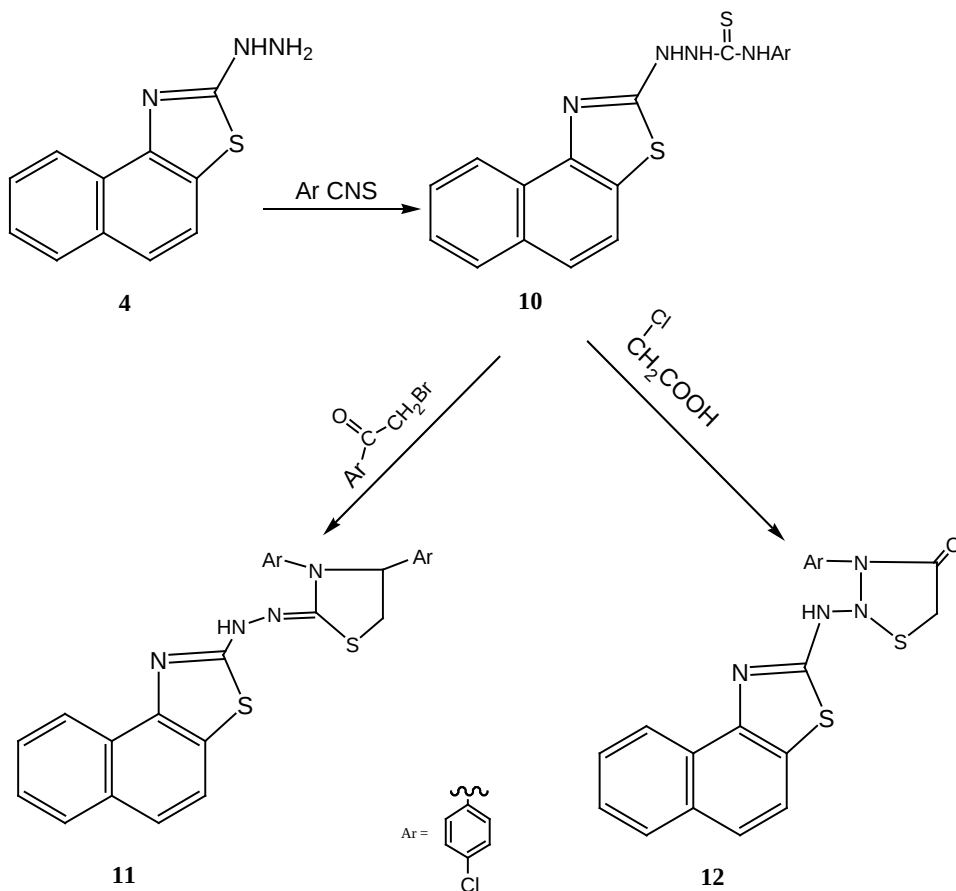
respectively. Also, hydrazino thiazolo derivatives **4** was reacted with diethyl malonate to afford thiazolo pyrimidino derivative **7**. Reaction of hydrazino thiazolo derivatives **4** with benzelidine derivatives gave thiazolo pyrimidino derivative **8** and **9**. (Scheme 2).



Scheme 2

Scheme2: Synthetic route of compounds **5** - **9**

Additionally, the compound **4** was reacted with p. chloro phenyl isothiocyanate afforded compound **10**. Compound **10** reacted with p.chloro phenacyl bromide and chloro acetic acid respectively to afford thiazolo and thiadiazolo derivatives **11** and **12** respectively (Scheme 3).



Scheme 3: Synthetic route of compounds **10** - **12**

Anti-Microbial Activity

The tested compounds **4**, **5**, **6**, **7**, **8**, **9**, **11** and **12** were evaluated *in vitro* for their anti-microbial activity. The antimicrobial activities are carried out against three bacterial strains, (*Staphylococcus aureus*, *Staphylococcus epidermidis* and *Escherichia coli*), and three fungal strains (*Aspergillus fumigates*, *Aspergillus niger* and *Alternaria alternata*). The preliminary screening results indicated that the most compounds showed antimicrobial activity from weak, moderate to good. From the inhibition zone diameter data analysis, compounds **4**, **8** and **9** showed good inhibitions against all the species of bacterial but compounds **8** and **9** moderate inhibitions against *A. niger* and *A. alternata*. Compounds **5**, **6** and **7** showed in general weak inhibitions against all the species of bacterial and fungal strains. Compounds **11** and **12** showed in general moderate inhibitions against all the species of bacterial and fungal strains, but compound **12** showed good inhibition against *A. alternata* (Table 1). Many studies reported antimicrobial activities

of thiazolo pyrimidine derivatives (Habib et al, 2007; Rashad et al, 2010; Kotaiah et al, 2012).

Table 1: The Antimicrobial activity of tested compounds at 100 µg/ml concentrations

Compd. NO.	Diameter of the inhibition zone ^a (mm)					
	Bacteria			Fungi		
	<i>S. aureus</i>	<i>S. epidermidis</i>	<i>E. Coli</i>	<i>A.Fumigates</i>	<i>A. niger</i>	<i>A. Alternata</i>
4	27	25	24	21	20	22
5	15	10	7	9	11	8
6	10	9	5	12	9	10
7	12	9	10	13	12	15
8	23	22	26	20	18	17
9	25	23	20	21	19	19
11	16	18	16	15	17	18
12	18	19	19	17	17	20
Tetracycline _b	29	26	28	-	-	-
Ketoconazole _e	-	-	-	20	19	23

^a15mm or less weak inhibition, 16-20mm: moderate inhibition, 20mm or more: good inhibition

^bThe concentration of used standard drugs was 30 µg/mL

The Minimum Inhibitory Concentration (MIC)

The minimum inhibitory concentration (MIC, µg/ ml) of the most active compounds **4,8** and **9** against two species of bacteria (*S. epidermidis* and *E. coli*) and also two species of fungi (*A. niger* and *A. alternata*) were determined (Table 2). Compounds **4, 8** and **9** demonstrated good inhibitions against the selected bacterial and fungal strains.

Table2: The minimum inhibitory concentration (MIC, µg/ml) of tested compounds 4, 8 and 9

The selected organisms	The minimum inhibitory concentration (MIC)			
	4	8	9	Standard^a
<i>S. aureus</i>	0.48	0.53	0.64	0.45
<i>E. coli</i>	0.34	0.60	0.53	0.37
<i>A. niger</i>	0.19	0.16	0.12	0.25
<i>A. alternata</i>	0.46	0.39	0.41	0.30

^aTetracycline and Ketoconazole were used as standard drugs against bacterial and fungal strains, respectively.

Cytotoxicity Activity

The LC₅₀ values of tested compounds **4,8** and **9** were found to be 3.23, 5.14 and 2.22µg/ ml, respectively (Table 3). The standard drug Bleomycin has LC₅₀ value at 0.41 g/ml. The lowest LC₅₀ value was found in the case of compound **8** indicating higher cytotoxicity than the other compounds. Compounds **4** and **9** showed potent biocidal activity against brine shrimp due to their lower cytotoxicity that agreement with preliminary anti-microbial screening and the minimum inhibitory concentration (MIC).

Table3: Cytotoxicity activity of tested compounds 4, 8 and 9

Comp. No	95% confidence limit ppm			Regression Equation	X ² (df)
	LC ₅₀	Lower	Upper		
4	3.23	2.08	6.02	Y=3.98 + 1.85 X	3.38 (2)
8	5.14	4.15	10.15	Y=3.17 + 2.27 X	0.35 (2)
9	2.22	1.30	4.10	Y=4.36 + 1.78 X	0.32 (2)
Bleomycin ^a	0.41	0.27	0.62	Y=3.16 + 1.98 X	0.62 (2)
Gallic Acid ^a	4.56	3.35	6.12	Y=3.93 + 1.62 X	1.25 (2)

^aBleomycin and gallic acid were used as standard drugs in cytotoxicity activity.

Structure Activity Relationship

Structure activity relationships based on the obtained results indicated that, substitution of pyrimidine derivatives have anti-microbial activity. Compounds **4**, **8** and **9** have high anti-microbial activity due to presence of electron-donating moiety which increase the pharmacological activity. This makes the sequence of ruling anti-microbial properties regarding substitution of electron –donating group in pyrimidine derivatives as, hydrazine > amino ethoxy carbonyl > amino cyano as exhibited in compounds **4** > **8** > **9** respectively. Compounds **11** and **12** have moderate anti-microbial activity due to presence of hydrazino thiazole attached with electron-withdrawing moiety which decrease the pharmacological activity. This makes the sequence of ruling anti-microbial properties regarding substitution of electron-withdrawing group in pyrimidine derivatives as, carbonyl adjacent to phenyl > diphenyl as exhibited in compounds **12** > **11** respectively. Also, compounds **5**, **6** and **7** have week anti-microbial activity due to presence of electron-withdrawing moiety which decrease the pharmacological activity. This makes the sequence of ruling anti-microbial properties regarding substitution of electron-withdrawing group in pyrimidine derivatives as, carbonyl of imidazole > dicarbonyl of pyrimidine > phenyl of imidazole as exhibited in compounds **5** > **7** > **6** respectively.

Conclusion

The objective of the present study was to synthesize and investigate the anti-microbial activity of new thiazolo pyrimidine derivatives. The starting material **2** was synthesized and carried out to synthesize thiazolo derivatives **4**. Compound **2** carried out to synthesize imidazolo thiazolo derivative **5**, **6** and thiazolo pyrimidino derivative **7**, **8** and **9** respectively. Compound **4** was carried out to synthesize of compound **10**. Compound **10** was carried out to synthesize of triazolo thiazolo and thiadiazolo derivatives **11** and **12** respectively. The newly tested synthesized compounds **4**, **5**, **6**, **7**, **8**, **9**, **11**, **12** and the standard drug Tetracycline and Ketoconazole were found to exhibit essentially equipotent anti-microbial activity.

Results are suggesting thiazolo pyrimidine derivatives emerge as valuable compounds with great potential to be used as antibacterial and antifungal agents, and as promising candidates for further efficiency evaluation.

Studying of biodegradability property of the produced thiazolo pyrimidine derivatives would be of great value for protecting and preserving the environment.

Many studies reported successful biological degradation of many synthesized compounds (Daniel et al, 1999; El-Arnaouty et al, 2008; Shah et al, 2008; Abd El-Mohdy and Ghanem, 2009).

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