Synthesis and Antimicrobial Screening of New Sulfonamides bearing Pharmacologically Active Components

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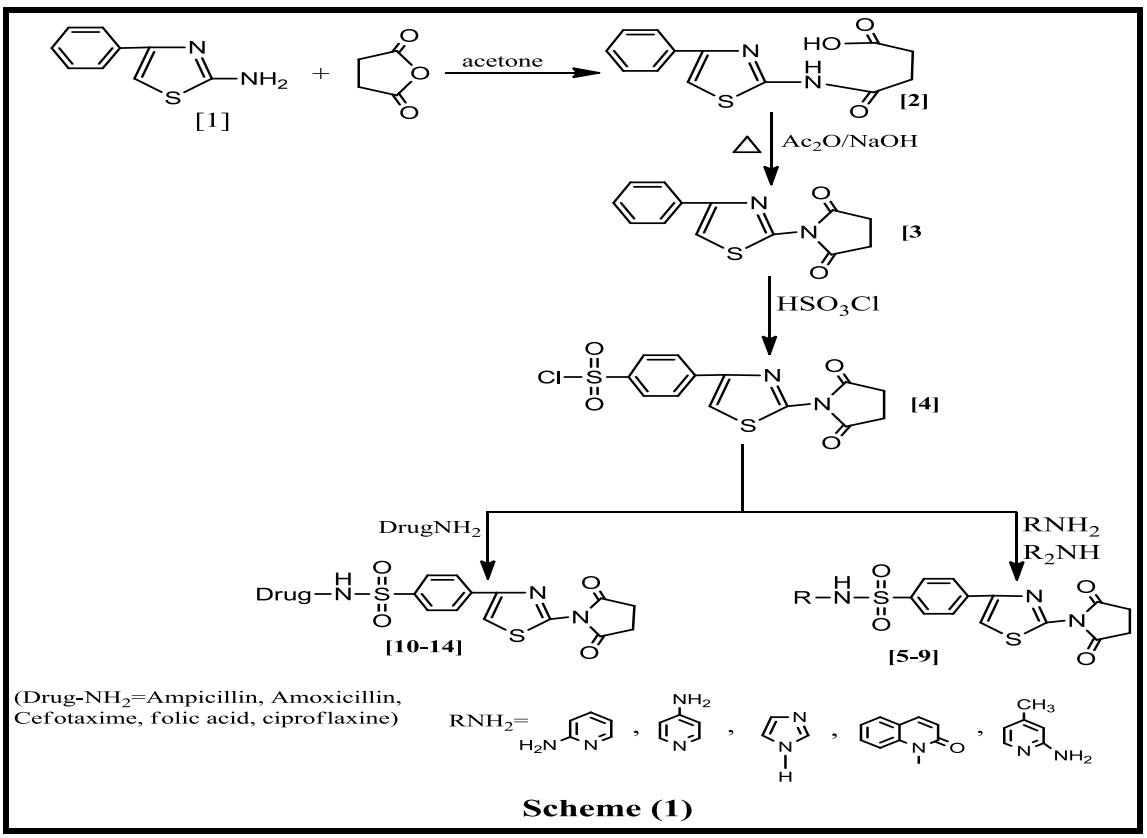
Abstract

In this work, several new sulfonamides linked to biologically active heterocycles namely were prepared. Preparation of the new slfonamides was performed via multistep synthesis. In the first step 2-amino-4-phenyl thiazole was introduced in reaction with sucsunic anhydride in glacial acetic acid under reflux condition producing compound[2] N-(4-phenyl thiazole-2-yl) succinic acid which in turn introduced in ring closer reaction by fusion in the second step producing compound N-(4-phenyl thiazole-2-yl) succinimide and this subssequently introduced in reacation with chlorosolfonel chlorid affording compound[3] of 4-[2-(N-succinimidyl) thiazole-4-yl] phenylsulfonyl chloride. Compound[4] reprsents the parent synthone from which all the target slfonamides drivitves were synthesized via following different synthetic paths. Antimicrobial activities of the prepared imides were evaluated and the results indicated that most of them possess high antimicrobial activity.

Keywords: Heterocycles membered rings, sulfonamide, antimicrobial activity, drugs.

Introduction

Since sulfonamides are known biologically active compounds having wide spectrum of medicinal and chemotherapeutic applications, this part involved using of new strategy for preparation of the desired new heterocyclic derivatives.[1,4] The new strategy was performed via synthesis of heterocyclic amine substituted with phenyl ring (4-phenyl-2-amino thiazole), then this amine was introduced in reaction with cyclic anhydride (succinic anhydride) producing new compound containing both thiazole ring and cyclic imide,[8,10] then this compound was introduced in chloro sulfonation producing sulfonyl chloride derivative[3,5] which in turn attacked amino group either in heterocyclic amines or in selected drug molecules producing new heterocyclic derivatives containing three active components including cyclicimide, five or six–membered heterocycles and sulfonamide moieties present simultaneously in the same molecule.



Scheme 1: The syntheses performed

Material and Methods

Uncorrected melting points were recorded on Gallenkamp melting point apparatus. SHIMADZN FTIR-8400 Fourier Transform Infrared spectrophotometer was used for recording FTIR spectra of the prepared compounds. Bruker ultrasheild 300 MHz apparatus was used for recording ^{1}H-NMR and ^{13}C-NMR spectra using DMSO-d_6 as solvent and TMS as internal standard. Hetashi model incubator was used for antimicrobial activity evaluation.

This part involved synthesis of several new sulfonamides containing both succinimide moiety and heterocycles including pyridine and quinoline. Also in this part new sulfonamides are linked to both succinimide moiety and drug molecule including Amoxicillin, Ampicillin, Cefotaxime, Folic acid and Ciproflaxine were synthesized. Synthesis of all sulfonamides in this part was based on 2-amino-4-phenylthiazole.

Preparation of 2-amino-4-phenyl thiazole [1]: The titled compound [1] is synthesized via reaction of equimolar amount of acetophenones and thiourea in the presence of iodine. The separated aminothiazole was filtered, washed with water, dried and recrystallized form water-alcohol.

Preparation of N-(4-phenyl thiazole-2-yl) succinamic acid[2]: The titled compound [2] was prepared by following the same method used in preparation of compounds [2] except using of compound [1] instead of drug and succinic anhydride instead of phthalic anhydride.

Preparation of N-(4-phenyl thiazole-2-yl) succinimide [3]: The titled compound [3] was synthesized by dehydration of compound [2] either by fusion or by using dehydrating agen.

Preparation of 4-[2-(N-succinimidyl) thiazole-4-yl] phenylsulfonyl chloride [4]: The titled compound was prepared according to the literature with some modifications. Chlorosulfonic acid (5 mL) was placed in a suitable round bottomed flask equipped with thermometer and dropping funnel containing (0.01 mol, 2.58 g) of N-(4-phenyl thiazole-2-yl) succinimide dissolved in (30 mL) of chloroform. Flask content was cooled to 0°C, then imide solution was added drop wise at such a rate that temperature of the well stirred mixture did not rise above 5°C. When addition was complete, the reaction mixture was stirred for four hrs., then was allowed to stand overnight in the refrigerator. The resulted mixture was poured onto crushed ice with stirring and the obtained oily layer was purified by recrystallization from petroleum ether. Physical properties of compounds [4] are listed in table 1.

Preparation of 4-[2-(N-succinimidyl) thiazole-4-yl] phenyl sulfonamido pyridine or quinoline or picoline or Imidazole [5-9]: 0.01 mol of heterocyclic amine (amino pyridines or 1-amino-2-oxo-quinoline or 2-amino picoline or imidazole) was dissolved in 30 mL of dry pyridine, then 0.01 mol, 3.71 g of compound [4] was added with stirring and keeping temperature below 40°C.

The resulted mixture was refluxed for three hrs with continuous stirring, then was cooled to room temperature and poured into excess cold water with stirring. The obtained precipitate was filtered, washed with water, dried and recrystallized from a suitable solvent.

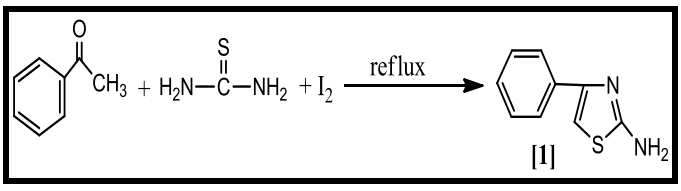
Preparation of4-[2-(N-succinimidyl)thiazole-4-yl]phenyl sulfonamido drug [10-14]: (Amoxicillin, Ampicillin, Cefotaxime, Ciproflaxine or Folic Acid). The titled compounds [10-14] were prepared by following the same method used for preparation of compounds [5-9] except using of drugs including Amoxicillin, Ampicillin, Cefotaxime, Ciproflaxine or Folic Acid instead of heterocyclic amines. The obtained product was recrystallized from a suitable solvent. Physical properties of compounds [5-14] are listed in table 2 and 3.

Biological activity study: Mulerhonton agar was added to one liter of distilled water in suitable conical flask with stirring and heating until complete dissolving, then the flask was stopperd by cotton and the medium was sterilized in an autoclave for 20 minutes at 121°C under pressure of 15 bound/inch.

The medium was cooled to 45-55°C and then placed in Petri dishes about 20 mL for each one and was left to cool and solidified. The studied bacteria and fungi were placed on the nutrient agar surface, then by using a sterilized cork borer cups were scooped out of agar medium contained in a Petri dish and the test compound solution (0.1mL) was added in the cups and the Petri dishes were subsequently incubated at 37°C for 48 hrs.[3,5] Ampicillin and fluconazole were used as reference drugs and DMF as a negative control. Zones of inhibition caused by the various prepared compounds were determined and the results are listed in table 7.

Results and Discussion

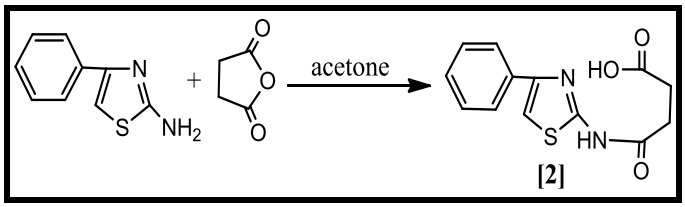
2-Amino-4- phenyl thiazole [1]: Compound [1] was prepared according to literature procedure[6,7] via reaction of acetophenones and thiourea in the presence of iodine under reflux condition.



Physical properties and spectral data of compound [1] are fitted with those reported in literatures.

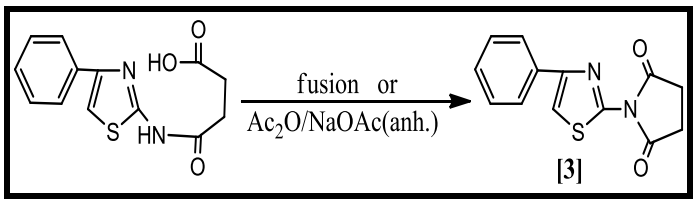
N-(4-phenyl thiazole-2- yl) Succinamic acid [2]: Compound [2] was prepared via reaction of compound [1] with succinic anhydride in acetone as solvent. Mechanism of

this reaction involved nucleophilic attack of amino group in compound [1] on carbonyl group in succinic anhydride following the same mechanism steps as shown in scheme 2.



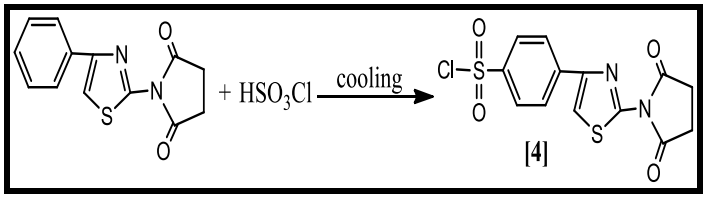
Compound [2] was afforded as yellow solid in 92% yield having melting point 148-150°C. FTIR spectrum of compound [2] showed absorption bands at 3360 cm^{-1} due to ν(O-H) carboxylic and ν(N-H) amide. Absorption bands due to ν(C-H) aromatic and ν(C-H) aliphatic appeared at 3058 cm^{-1} and 2950 cm^{-1} while absorption bands due to ν(C=O) carboxyl and ν(C=O) amide appeared at 1708 cm^{-1} and 1635 cm^{-1}. Other absorption bands appeared at 1596 cm^{-1}, 1571 cm^{-1} and 634 cm^{-1} which belong to ν(C=N), ν(C=C) aromatic and ν(C-S) respectively.

N-(4-phenyl thiazole-2- yl) Succinimide [3]: Compound [3] was prepared via dehydration of compound [2] by using either fusion method or by using acetic anhydride and anhydrous sodium acetate as dehydrating agent following the same mechanism steps shown in scheme (3).



Compound [3] was afforded as gray solid in 90% yield having melting point 179-180°C. FTIR spectrum of compound [63] showed disappearance of absorption band belonging to ν(O-H) carboxylic and ν(N-H) amide. The spectrum showed also absorption bands at 1731 cm^{-1} 1716 cm^{-1}, 1697 cm^{-1} and 1689 cm^{-1} which are due to asym. and sym. ν(C=O) imide, ν(C=N) thiazole and ν(C=C) aromatic respectively. Other absorption bands appeared at 3020 cm^{-1}, 1311 cm^{-1} and 638 cm^{-1} which belong to ν(C-H) aromatic, ν(C-N) imide and ν(C-S) thiazole.

4-[2-(N-succinimidyl) thiazole-4-yl] phenylsulfonyl chloride [4]: Compound [4] was prepared via introducing of compound [3] in reaction with chlorosulfonic acid under certain conditions.



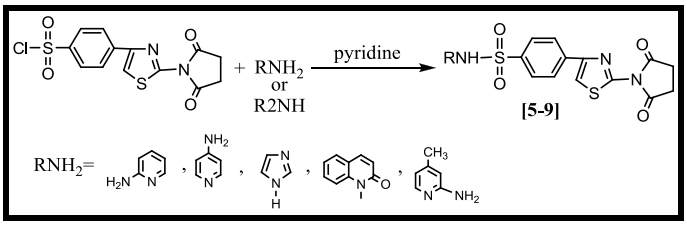
Mechanism of this reaction involved electrophilic substitution reaction of electron-deficient sulfur atom in HSO_3Cl on -p-position of phenyl ring in compound [3] followed by elimination of water molecule as shown in scheme 2.

Compound [4] was afforded as pale yellow solid in 70% yield having melting point 126-128°C. FTIR spectrum of compound [4] showed clear absorption bands at 1722 cm^{-1}, 1600 cm^{-1} and 1589 cm^{-1} due to ν(C=O) imide, ν(C=N) thiazole and ν(C=C) aromatic respectively. Absorption bands belong to asym. ν(SO_2) and sym. ν(SO_2) appeared at 1350 cm^{-1} and 1205 cm^{-1}. While bands due to ν(C-H) aromatic, ν(C-N) imide and ν(C-S) thiazole appeared at 3091 cm^{-1}, 1298 cm^{-1} and 642 cm^{-1}.

Compound [64] represents the important starting material containing sulfonyl group and can be introduced successfully in reaction with heterocyclic amines in the next step producing the desired compounds containing both succin imide and hetero ring or (Drug molecules) linked together through sulfonamido group.

Physical properties of compounds [2-4] are listed in table 1 while their FTIR spectral data are listed in table 2.

4-[2-(N-succinimidyl) thiazole-4-yl] phenyl Sulfonamido (Pyridine, Imidazole, quinoline) [5-9]: The titled compounds were prepared via reaction of compound [4] with different heterocyclic amines involved (2-amino pyridine, 4-amino pyridine, imidazole, 1-amino-2-oxoquinoline and 4-methyl-2-amino pyridine) in dry pyridine.



This reaction represents nucleophilic substitution reaction and its mechanism involved nucleophilic attack of amino group in heterocyclic amine on sulfur atom in compound [4] followed by elimination of HCl molecule as shown in scheme 3.

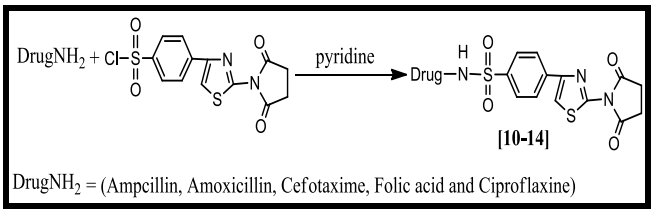
Physical Properties of compounds [6-9] are listed in table 3.

FTIR spectrum of compound [5-9] showed absorption bands at (3193-3344) cm^{-1}, (3006-3060) cm^{-1} and (2905-2923) cm^{-1} due to ν(N-H), ν(C-H) Aromatic and ν(C-H) aliphatic respectively. Absorption bands belong to ν(C=O) imide, ν(C=N) and ν(C=C) aromatic appeared at (1643-1679) cm^{-1} (1575-1627) cm^{-1} and (1542-1595) cm^{-1}. While bands due to asym. ν(SO_2) and sym. ν(SO_2), ν(C-N) imide and ν(C-S) thiazole appeared at (1325-1375) cm^{-1}, (1126-1170) cm^{-1}, (1263-1396) cm^{-1} and (619-700) cm^{-1} respectively. ^{1}HNMR

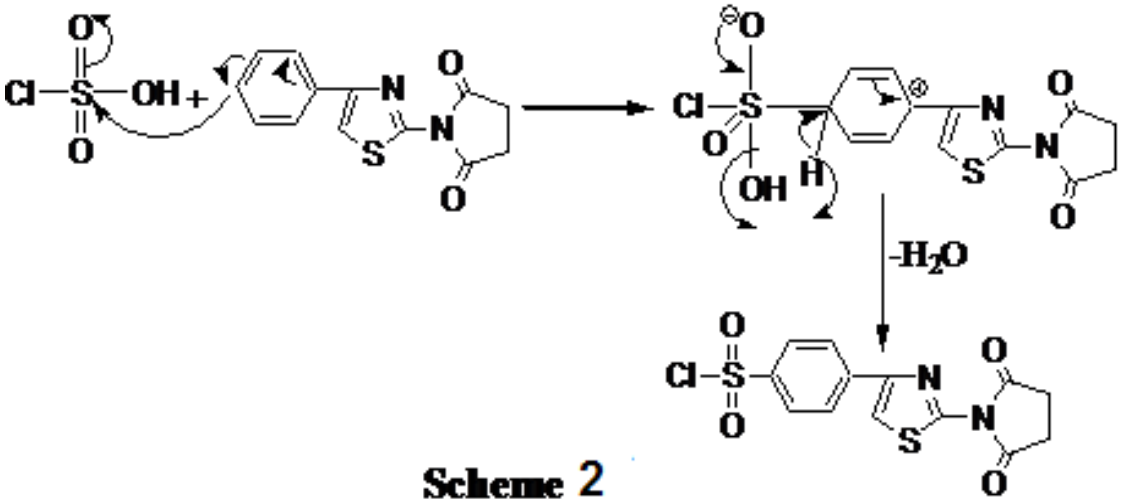
spectrum of compound [6] showed signal at δ=2.8 ppm belonging to CH_2-CH_2 protons, signals at δ=7.07 ppm belonging to aromatic protons and thiazole protons and signal at δ=7.74 ppm belong to imidazole protons.

^{13}CNMR spectrum of compound [6] showed signal at (δ=30) ppm belonging to (CH_2-CH_2) carbons, signals at (δ=108-129.2) ppm belonging to aromatic carbons and signals at (δ=135.7) ppm belonging to (C=C) carbons in thiazole and imidazole rings. Other signals appeared at (δ=150.6, 158.1 and 172.5) ppm which belong to (C=N) thiazole, (C=N) imidazole and (C=O) imide carbons respectively.

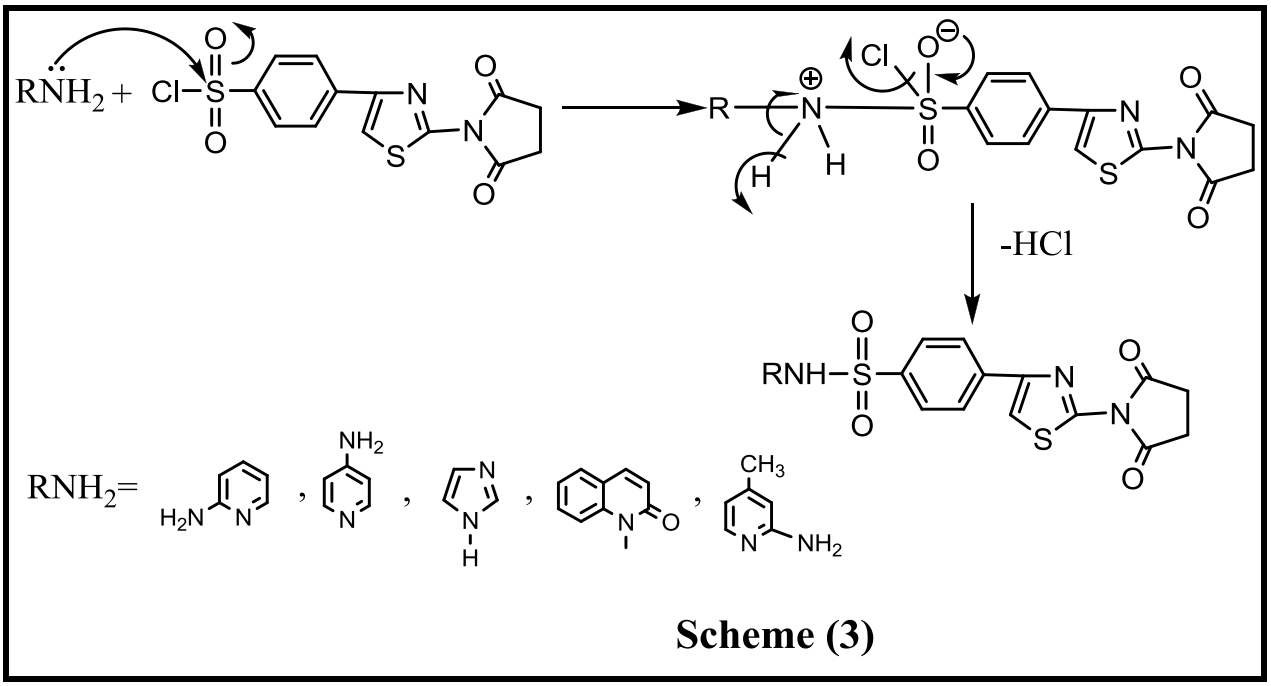
4-[2-(N-succinimidyl) thiazole-4-yl] phenyl Sulfonamido (Ampcillin, Amoxicillin, Cefotaxime, Folic Acid and Ciproflaxine) [10-14]: Compounds [10-14] were prepared via reaction of compound [4] with different drug molecules including (Ampcillin, Amoxicillin, Cefotaxime, Folic Acid and Ciproflaxine) in dry pyridine.



Mechanism of this reaction involved nucleophilic attack of amino group in Drug on sulfur atom in compound [64] followed by elimination of HCl molecule following the same steps described in scheme.



Scheme 2



Scheme (3)

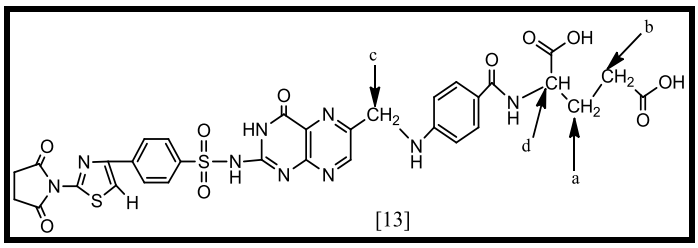
Physical properties of compounds [10-14] are listed in table 4 while FTIR spectral data are shown in table 5. FTIR spectra of compounds [10-14] showed absorption bands at (3274-3527) cm^{-1}, (3261-3377) cm^{-1}, (3062-3080) cm^{-1} and (2923-2979) cm^{-1} due to ν(O-H) carboxylic, ν(N-H) amide, ν(C-H) aromatic and ν(C-H) aliphatic respectively. Absorption bands belong to ν(C=O) imide, ν(C=O) (carboxyl, amide), asym. $\nu(SO_2)$ and sym. $\nu(SO_2)$ appeared at (1650-1710) cm^{-1}, (1625-1685) cm^{-1}, (1338-1375) cm^{-1} and (1143-1178) cm^{-1} and (603-700) cm^{-1} while absorption bands due to (ν(C=N), ν(C=C)), ν(C-N) imide and ν(C-S) appeared at (1541-1606) cm^{-1}, (1299-1360) cm^{-1} and (603-700) cm^{-1} respectively. FTIR spectrum of compound [72] showed also absorption bands at 1737 cm^{-1} and 1199 cm^{-1} belonging to ν(C=O) ester and ν(C-O) ester, while compound [11] showed absorption bands at 3440 cm^{-1} and belong toν(O-H) phenolic.

^{1}HNMR spectrum of compound [11] showed signals at (δ=1.2-1.4) ppm belonging to two (CH_3) protons, signal at (δ=1.6) ppm belongs to benzylic proton and signals at (δ=2.6-2.7) ppm belongs to (CH_2-CH_2) protons. signal appeared at (δ=3.5) ppm belong to thiazole ring proton.

While signals at(δ=4.6-4.8) ppm belong to azitidine and thiazine rings protons. Signal at (δ=5.1) ppm belongs to (O-H) phenolic proton, signals at (δ=6.7-7.8) ppm belong to aromatic protons, signal at (δ=8.57) ppm belongs to (N-H) amide protons and signal at (δ=12.25) ppm belongs to (O-H) carboxylic proton.

^{13}CNMR spectrum of compound [11] showed signal at (δ=24-29) ppm belonging to two (CH_3) groups and (CH_2-CH_2) carbons, signals at (δ=58 and 59) ppm belong to benzyl carbon and carbon atom in thiazine ring that bonded to methyl groups and signals at (δ=115 and 115.34) ppm belong to two azitidine ring carbons and carbon in thiazine ring linked to carboxyl group.

Signal at (δ=124.38) ppm belongs to (C=C) carbons in thiazole ring and signals at (δ=126.12-129.17) ppm belong to aromatic carbons. Other signals appeared at (δ=136.63, 150.02, 158, 170.68 and 171) ppm belonging to (C=N) thiazole, (C=O) in azitidine ring, (C=O) amide, (C=O) carboxyl and (C=O) imide carbons respectively.



[13]

^{1}HNMR spectrum of compound [13] showed signals at δ=(1.8-2)ppm belonging to (CH_2 a) protons, signals at (δ=2.1-2.3) ppm belong to (CH_2 b) protons and signals at (δ=2.8) ppm belong to (CH_2-CH_2) Succinimide protons. Signals at δ=(4.8-4.9) ppm belong to (CH_2c) protons and (CHd) proton, while signal appeared at (δ=5.9) ppm belongs to thiazoleanddiazene rings protons. Other signals appeared at δ=(6.8-7.7), (8.1-8.7) and (10.1,11.9) ppm which belong to aromatic protons, (NH) protons and (OH) carboxyl protons respectively.

^{13}CNMR spectrum of compound [13] showed signals at (δ=23.2-24.4) and (25.1-26.7) ppm which belong to (CH_2 a) carbon and (CH_2-CH_2) succinimide carbons. Signals at (δ=31.1) ppm belong to (CH_2b) carbon, signals at (δ=53.5-62.98) ppm belong to (CH_2c) and (CHd) carbons and signals at (δ=88.3-128.8) ppm belong to aromatic carbons. signals at (δ=129.07-129.7) ppm belong to (C=C) carbons in thiazole and diazine rings and signals appeared at (δ=138.33 and153.9) ppm belong to(C=N) carbons. Other signals appeared at (δ=155.37, 168 and 175.6) ppm which belong to (C=O) amide, (C=O) carboxyl and (C=O) imide carbons respectively.

Figures 1 to 9 showed FTIR spectra while figures 10 to 12 showed ^{1}HNMR and ^{13}CNMR spectra for some of the prepared compounds in this part.

Inhibition Zones of the Prepared Compounds [2-14]: The newly synthesized compounds [2-14] were tested for their *in vitro* antimicrobial activity against four types of bacteria including *Staphylococcus aureous, Streptococcus pyogenes, E. coli* and *Klebsiellapneumonia*e and *Candida albicans fungi* by using cup plate method. Zones of inhibition caused by each compound were measured in (mm) and the results are listed in table 7.

The results indicated that compound [5] has very high activity of inhibition against *Klebsiella pneumoniae, S.pyogenes and E.coli* and high activity of inhibition against *S.aureous.* Compounds [2, 3, 4, 6] showed modreate activity of against *Candida albicans fungi.* Compounds [66, 67] showed modreate activity against *S.aureous while* compound [19] showed high activity against *S.aureous* and *Klebsiella pneumoniae.* Other compounds were found to be slightly or weak active against the tested organisms.

The results indicated that compounds [10, 11] have very high activity of inhibition against *S. aureou*s and *Klebsiella pneumoniae* and high activity of inhibition against *S. pyogenes, E. coli* and *Candida albicans fungi.*

Compounds [12, 14] showed high activity of inhibition against *S. aureous* and showed modreate activity against S. *pyogenes, E. coli* and *Klebsiella pneumoniae*. Compound [13] showed weak activity against the tested organisms and compound [14] showed moderate activity against Candida albicans fungi.

Table 1
Physical properties of the prepared compounds [2-4]

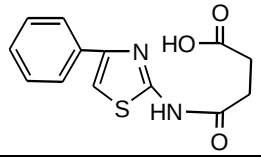
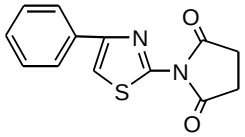
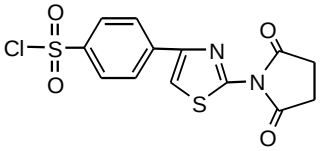
Comp. No.	Compound structure	Color	Melting Points °C	Yield %	Recrystallization Solvent
2		yellow	148-150	92	Benzene
3		gray	179-180	90	Acetone
4		pale yellow	126-128	70	Ethanol

Table 2
Physical properties of the prepared compounds [5-9]

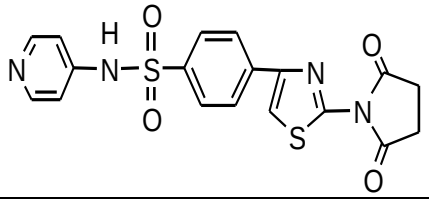
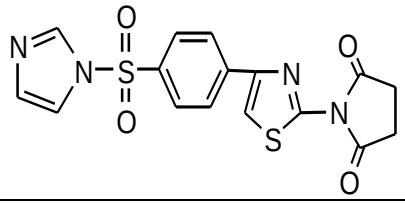
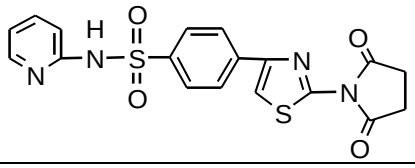
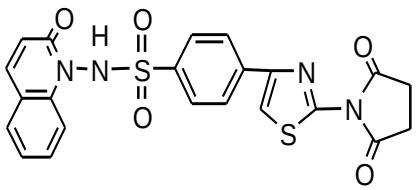
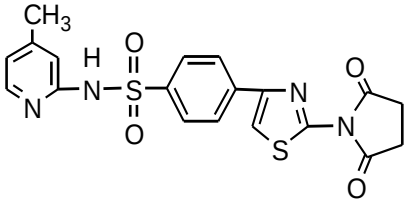
Comp. No.	Compound structure	Color	Melting Points °C	Yield %	Recrystallization Solvent
5		White	206-208	92	Ethanol
6		pale yellow	88-90	71	Methanol
7		White	102-104	60	n-hexane
8		Redish brown	192-195	82	Ethanol
9		pale yellow	68-70	55	n-hexane

Table 3
Physical properties of the prepared compounds [10-14]

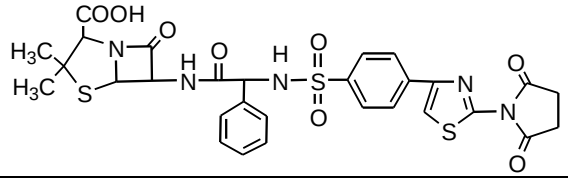
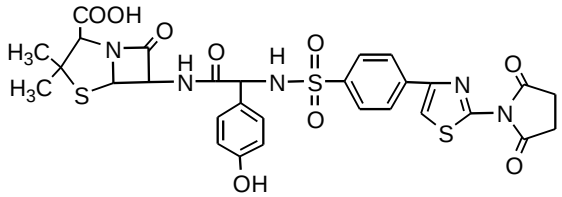
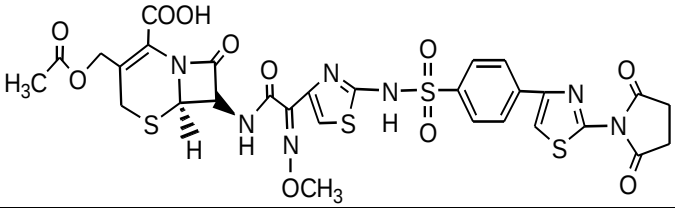
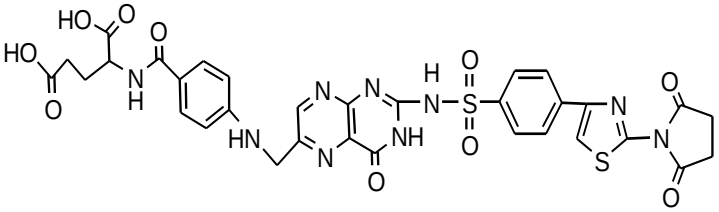
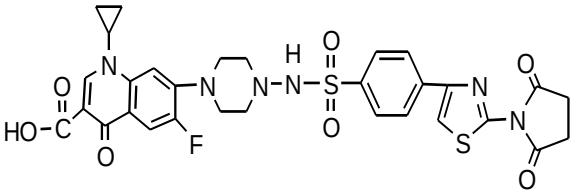
Comp. No.	Compound structure	Color	Melting Points °C	Yield %	Recrystallization Solvent
10		Yellow	220-223	60	Acetone
11		Pale Brown	108-110	78	Methanol
12		Brown	300.Dec	65	Acetone
13		Dark Yellow	273-270	63	Ethanol
14		White	Dec.320	70	n-hexane

Table 4
FTIR Spectral data of the prepared compounds [12-14]

Comp No.	ν(O-H) Carboxylic ν(N-H) Amide	ν(C-H) aromatic And aliphatic	ν(C=O) Carboxylic	ν(C=O) Amide	ν(C=N)	ν(C=C)	ν(C-S)
12	3360	3058 2950	1708	1635	1596	1571	634
Comp. No.	**ν(C-H) aromatic And aliphatic**	**ν(C=O) Imide**	**ν(C=N)**	**ν(C=C)**	**ν(C-N) Imide**	**ν(C-S)**	**Others**
13	3020	1731asym 1716sym	1697	1689	1311	638	-
Comp. No.	**ν(C-H) aromatic**	**ν(C=O) Imide**	**ν(C=N)**	**ν(C=C)**	**Asym.ν(SO2) sym.ν(SO2)**	**ν(C-N) Imide**	**ν(C-S)**
14	3091	1722	1600	1589	1350 1205	1298	642

Table 5
FTIR Spectral data of the prepared compounds [5-9]

Comp. No.	FTIR spectral data cm^{-1}								
	ν(C-H) aromatic and aliphatic	**ν(N-H)**	**ν(C=O) Imide**	**ν(SO_2) Asym.**	**ν(SO_2) sym.**	**ν(C=N)**	**ν(C=C) aromatic**	**ν(C-N) Imide**	**ν(C-S)**
5	3006 2923	3344 3299	1643	1371	1126	1627	1558	1396	619
6	3020 2910	-	1670	1325	1147	1575	1542	1263	659
7	3055 2918	3326 3193	1679	1375	1170	1618	1558	1325	696
8	3060	3250	1670	1371	1161	1608	1595	1296	700
9	3049 2905	3187	1676	1362	1132	1600	1554	1313	672

Table 6
FTIR Spectral data of the prepared compounds [10-14]

Comp. No.	FTIR spectral data cm^{-1}											
	ν(O-H) Carboxylic	**ν(N-H) amide**	**ν(C-H) Aromatic And aliphatic**	**ν(C=O) Imide**	**ν(C=O) Carboxylic And amide**	**ν(SO_2) Asym.**	**ν(SO_2) sym.**	**ν(C=N) ν(C=C) aromatic**	**ν(C-N) imide**	**ν(C-S)**	**ν (N-H) sulfon amide**	**Others**
10	3417	3307 3294	3062 2968	1705 1650	1637	1371	1159	1541	1338	700	3907	-
11	3296	3261	3068 2968	1670	1627	1371	1176	1542	1360	680	3890	ν(O-H) Phenolic 3440
12	3411	3263	3066 2979	1672	1637	1375	1163	1544	1325	682	3940	ν(C=O) Ester 1737 ν(C-O) Ester 1199
13	3527	3377	3080 2925	1708	1625	1340	1143	1541	1320	603	3460	-
14	3274	-	3066 2923	1710	1685 1645	1338	1178	1606 1541	1299	680	3270	-

Table 7
Inhibition zones of antimicrobial activity of compounds [2-9] in mm

Comp. No.	Gram-positive bacteria		Gram-negative bacteria		Fungi
	Staphylococcus aureus	***Streptococcus pyogenes***	***Klebsiella pneumoniae***	***Escherichia coli***	***Candida albicans***
2	+	-	-	++	-
3	+	+	-	++	-
4	+	-	-	++	-
5	+++	++++	++++	++++	++
6	++	+	+	++	++
7	++	-	-	-	-
8	-	-	-	-	-
9	+++	+	+++	-	-
Ampicillin	+++	+++	+++	+++	-
Fluconazole	-	-	-	-	+++
DMSO	-	-	-	-	-

Table 8
Inhibition zones of antimicrobial activity of compounds [10-14] in mm

Comp. No.	Gram-positive bacteria		Gram-negative bacteria		Fungi
	Staphylococcus aureus	***Streptococcus pyogenes***	***Klebsiella pneumoniae***	***Escherichia coli***	***Candida albicans***
10	++++	+++	++++	+++	+++
11	++++	+++	++++	+++	+++
12	+++	++	++	++	-
13	+	+	+	+	-
14	+++	++	++	++	++
Ampicillin	+++	+++	+++	+++	-
Amoxicillin	++	+++	++	++	-
Cefotaxime	++	++	+++	+++	-
Folic acid	+	+	-	-	-
Cefradoxial	+	+	++	++	-
Fluconazole	-	-	-	-	+++
DMSO	-	-	-	-	-

The mechanism of destroying cell wall can happen by three methods:

1. Binding of the compounds with the peptide chains and formation of compound-binding proteins complex by destruction of L-Lys and D-Glu bonds, which will result in the change and distortion bacterial cell wall morphology.

2. Inhibition of trans peptides enzyme which is the enzyme that catalyzes the formation of transferase peptide bonds of the bacterial cell wall, which will lead to stop cell wall formation.

3. The action of Autolysins enzymes is produced by certain bacteria ,especially the gram positive bacteria such as cocci. These enzymes are used to repast and reform bacterial morphology when there is any defect.

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