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Synthesis, Characterization Of Thiazolidin-4-one, Oxazolidin-4-one And Imidazolidin-4-one Derivatives From 6-Amino-1, 3-dimethyluraciland Evaluation Of Their Antioxidant And Antimicrobial Agent

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Synthesis, Characterization of Thiazolidin-4-one, Oxazolidin-4-one and Imidazolidin-4-one Derivatives from 6-Amino-1,3-dimethyluracil and evaluation of their Antioxidant and Antimicrobial Agent

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ABSTRACT

In this study, a new series of 6-amino-1,3-dimethyluracil derivative with 6-(3-substituted *N*-benzylidene)-1,3-dimethyl pyrimidine-2,4-dione-6-yl derivatives which were synthesized by using one pot synthesis. The reaction of 6-amino-1,3-dimethyluracil and different aromatic aldehyde in ethanol yielded Schiff bases. In the subsequent step reaction of Schiff bases with 2-mercaptoacetic acid, 2-chloroacetic acid and 2-amino acetic acidn in Tetrahydrofuran yielded five membered heterocyclic rings of 6-amino-1,3-dimethyluracil derivative which includes: 2,3-thiazolidin-4-one, 2,3-oxazolidin-5-one, 2,3-imidazolidin-4-one derivatives. The structures of newly synthesized compounds were confirmed by their physicochemical and spectral means FTIR, ^{1}HNMR and ^{13}CNMR. The synthesized compounds were evaluated in vitro for antioxidant and antimicrobial activities against four types of bacteria and four types of fungi.

1. Introduction

Uracil and its derivatives are one of the most an important class of compounds because these molecules can act as both nucleophiles and electrophiles (Singh, 2019). Uracil's estimated that deamination of cytosine leads to up to 500 uracil residues in a single human cell each day, Besides uracil displays as antihyperthermophilic (Shi et al., 2019). Uracil derivatives have a extensively spectrum of pharmacological such as Anticancer and Antibacterial (Sanduja et al., 2020), Antioxidant (Nayab et al., 2020), Anti-leukemia (Długosz-Pokorska et al., 2020), Cytotoxicity and AntiHIV-1/2 (Novakov et al., 2020) and Antidiabetic (Spasov et al., 2019). In particular, thiazolidinone derivatives have drawn attention and have a wide range of biological properties, in addition to existing in the structure of many natural products (Genc Bilgicli et al., 2020). Thiazolidinones as cholinesterase

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inhibitors and promising compounds against memory decline in Alzheimer's disease, which is associated with cholinergic dysfunctions in rat brain (da Silva et al., 2020). Also thiazolidinone derivatives used as inhibits oesophageal cancer cell proliferation (Wang et al., 2020), anticervical cancer activity (Abbas and El-Karim, 2019), antitubercular agent (Deshmukh et al., 2019), Antibacterial (Cheddie et al., 2019), Anti-Toxoplasma (Abdizadeh et al., 2020), Anti-Cytotoxicity and Anti-inflammatory (Shawky et al., 2020) in addition of Anti-hepatitis-C (Hassan et al., 2019). Besides these, oxazolidinones are the latest class of inhibitory effects exerted on the mitochondrial function of megakaryoblastic cells appear to be particularly protracted (Milosevic et al., 2019) and treatment of skin and skin Structure infections (Santos et al., 2020). At the sametime, Imidazolidinones can improve the epidermal barrier function of facial skin, which is exposed to the sun on a daily basis(Iriyama et al., 2019). Anti-inflammatory and Analgesic activity (El-Sharief et al., 2019), Antiviral (Swain and Mohanty, 2019) and potent antileishmanial agents (Ramu et al., 2019).

EXPERIMENTAL:

Materials and Instruments

Chemicals used in this research are supplied from BDH, Fluka, Merck and Sigma Aldrich companies and used without further purification. In addition to melting points were uncorrected and registered by digital Stuart scientific SMP3 melting point device. While, Thin layer chromatography (TLC) used to check purity and homogeneity of synthesis compounds. FTIR spectra of the synthesized compounds in the (4000-600) cm^{-1} spectral range were recorded on SHIMAZU FTIR-8400 Fourier transform Infrared spectrophotometer using KBr discs. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on BRUKER 500MHz in Iran, instrument using TMS as internal reference and DMSO-d_6 as a solvent. Spectrophotometer were recorded by *Apel PD-303- spectrophotometer*, japan.

Synthesis of 6-(3-substituted *N*-benzylidene)-1,3-dimethyl pyramid-ine-2,4-dione-6-yl (1-6) (Al-Adhami and Al-Majidi, 2016)

A solution of (2.0 g, 0.0129 mol) 6-amino-1,3-dimethyluracil, (0.0129 mol) aromatic aldehydes in (15 mL) absolute ethanol solvent were mixed thoroughly with a catalytic (3-5) drops of glacial acetic acid, then the mixture refluxed in water bath up to (5-6) h., and the product was then dried, after evaporating the excess solvent and recrystallized from chloroform. Some of the physical properties and yield of compounds (1-6) are listed in Table (3.37).

Synthesis of 1,3-dimethyl-6-[2-(3-substituted phenyl) thiazolidin-4-one-3-yl]-pyrimidine-2,4-dione-6-yl (7-12) (Genc Bilgicli et al., 2020)

In this step, (0.0041 mol) of Schiff bases (**1-6**) and 2-mercaptoacetic acid (0.3 mL, 0.0041 mol) in THF (10 mL) was added gradually. The reaction mixture was then heated to reflux up on (18-20) h. After refluxing the reaction mixture was followed neutralized by addition of sodium bicarbonate solution 5% to remove unreacted 2-mercaptoacetic acid. The product was filtered and washed with water then further purification was done using recrystallized from ethanol. Some of the physical properties and yield of compounds (**7-12**) are listed in Table (3.45).

Synthesis of 1,3-dimethyl-6-[2-(3-substituted phenyl) oxazolidin-5-one-3-yl]-pyrimidine-2,4-dione-6-yl (13-18) (Al-Majidi and Hama, 2015)

Using a round bottom flask (50 mL), a mixture of (0.0021 mol) Schiff bases (**1-6**) in THF (10 mL) was added to a well-stirred solution of chloroacetic acid (0.2 g, 0.0021 mol) and mixed thoroughly with catalytic few drops of triethylamine in THF solvent. The solution was refluxed for (12-15) h., after cooling the solution, the crude precipitate was filtered and recrystallization using ethanol. Some of the physical properties and yield of compounds (**13-18**) are listed in Table (3.49).

Synthesis of 1,3-dimethyl-6-[2-(3-substituted phenyl) imidazolidine-4-one-3-yl]-pyrimidine-2,4-dione-6-yl (19-24) (Al-Majidi and Hama, 2015)

To a mixture of Schiff bases (**1-6**) (0.0021 mol) was stirred in (9 mL) of THF solvent, 2-aminoacetic acid (0.25 g, 0.0021 mol) in (5 mL) of THF was refluxed for (**16-20**) h. Then, the resulted mixture was filtered after cooling to room temperature, washed and recrystallized from acetone. Physical properties and yields of compounds (**19-24**) are listed in Table (3.53).

Table1- Physical properties and FTIR spectral data cm^{-1} of the synthesized compounds (1-6)

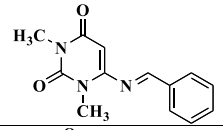
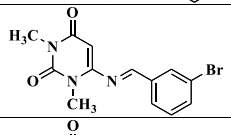
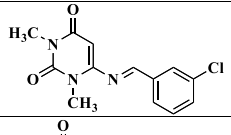
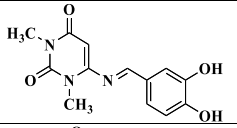
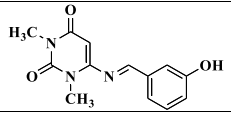
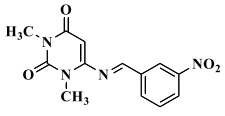
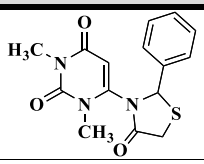
No.	Physical properties				Major FTIR Absorption cm^{-1}					
	Structure	M.P. °C	Yield %	Color	ν(C-H) Arom	ν(C-H) Aliph	ν(C=O) Amide	ν(C=N) ν(C=C) Olefinic	ν(C=C) Arom	Other bands
1		134-136	74	White	3006	2954	1733 1673	1654	1598 1585	-
2		179-181	76	Off White	3095	2956	1677 Overlap	1654	1610	-
3		140-142	85	White	3066	2956	1733 1668	1652	1610 1596	ν(C-Cl) 1163
4		138-140	88	White	3091	2927	1672 Overlap	1649	1604 1581	ν(O-H) 3332
5		158-160	71	White	3095	2952	1733 1679	1656	1616 1583	ν(O-H) 3357
6		192-193	90	Pale Yellow	3056	2956	1679 Overlap	1645	1614 1562	ν(NO_2) asym. 1514 sym. 1344

Table 2- Physical properties and FTIR spectral data cm^{-1} of the synthesized compounds (7-12)

No.	Physical properties				Major FTIR Absorption cm^{-1}					
	Structure	M.P. °C	Yield %	Color	ν(C-H) Arom	ν(C-H) Aliph	ν(C=O) Amide	ν(C=C)	ν(C-S)	Other bands
7		161-163	80	Brown	3022	2954 2889	1695	1583 1558	698	-

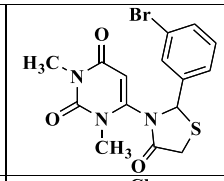
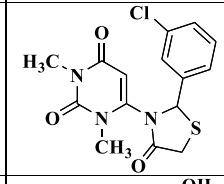
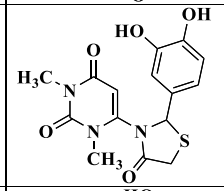
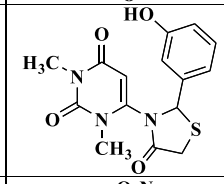
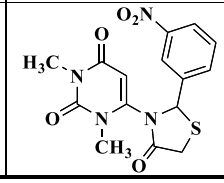
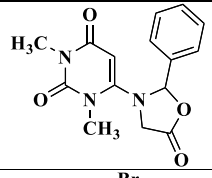
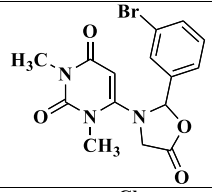
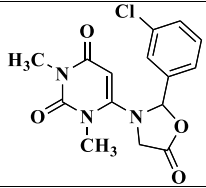
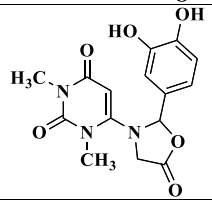
8		154-156	87	Pale Yellow	3068	2956 2935	1701 1674	1606	690	-
9		140-142	82	Pale Brown	3097	2956 2878	1681	1589	675	-
10		165-167	74	Brown	3088	2977 2819	1674	1589	709	ν(O-H) 3433
11		189-191	85	Pale Brown	3049	2964 2815	1676	1591	707	ν(O-H) 3427
12		175-177	71	Pale Yellow	3070	2956 2923	1701 1685	1608	705	ν(NO_2) asym.1500 sym. 1350

Table 3- Physical properties and FTIR spectral data cm^{-1} of the synthesized compounds (13-18)

No.	Physical properties				Major FTIR Absorption cm^{-1}					
	Structure	M.P. °C	Yield %	Color	ν(C-H) Arom	ν(C-H) Aliph	ν(C=O) Amide	ν(C=C)	ν(C-O)	Other bands
13		258-261	85	White	3097	2956 2821	1693 Overlap	1585	1249	-
14		201-203	80	White	3091	2952 2891	1689 Overlap	1598 1583	1245	-
15		182-184	82	Off White	3068	2950 2887	1730 1693	1583	1238	-
16		159-161	79	Off White	3065	2958 2827	1681 Overlap	1593	1247	ν(O-H) 3398

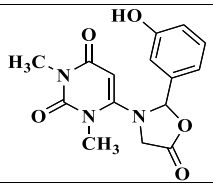
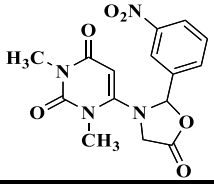
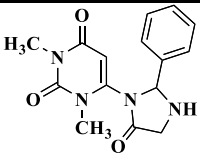
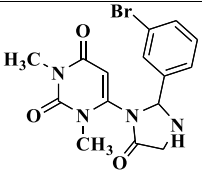
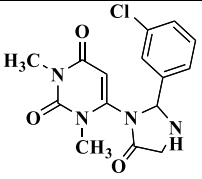
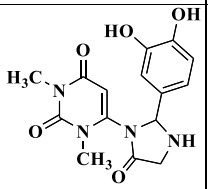
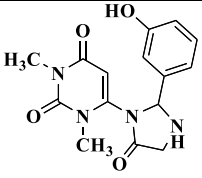
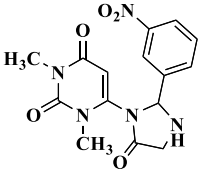
17		141-143	83	Pale Yellow	3096	2987 2954	1670 Overlap	1610 1593	1251	ν(O-H) 3398
18		226-228	91	Yellow	3053	2970 2889	1691 1674	1602	1251	ν(NO_2) asym.1500 sym. 1340

Table 4- Physical properties and FTIR spectral data cm^{-1} of the synthesized compounds (19-24)

No.	Physical properties				Major FTIR Absorption cm^{-1}					
	Structure	M.P. °C	Yield %	Color	ν(N-H)	ν(C-H) Arom	ν(C-H) Aliph	ν(C=O) Amide	ν(C=C)	Other bands
19		234-235	73	White	3342	3055	2972 2831	1731 1693	1585	-
20		214-216	84	Off White	3388	3055	2966 2825	1693 Overlap	1585	-
21		225-227	86	Off White	3230	3053	2950 2898	1708 1683	1585	-
22		181-183	85	Off White	3384	3056	2970 2889	1690 1679	1591	ν(O-H) 3461
23		213-215	76	White	3215	3055	2958 2831	1679 Overlap	1593	ν(O-H) 3394
24		241-243	90	Off White	3359	3066	2956 2921	1670 Overlap	1608	ν(NO_2) asym.1502 sym. 1334

Anti-microbial activity test (Teleb et al., 2019)

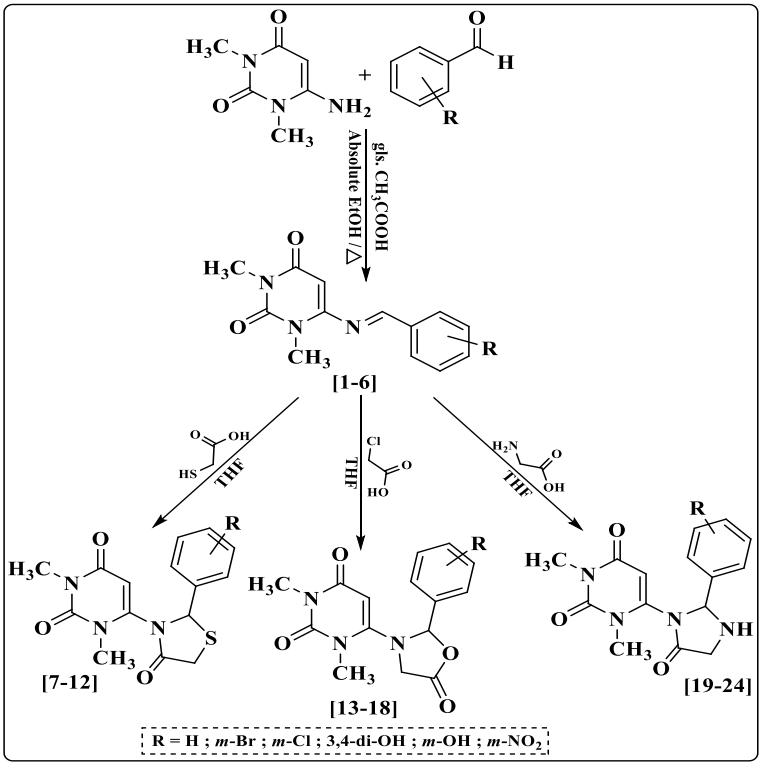
Anti-microbial activity test of the some synthesized compounds were performed according to "disk diffusion method". Number of the synthesized compounds had been evaluated on four bacterial strains, two Gram-positive bacteria (***Staphylococcus aureus*** and ***Staphylococcus epidermidis***) and two Gram-negative bacteria (***Escherichia coli*** and ***Klebsiella pnemonia***). They also evaluated on four fungal strains, yeast like pathogenic fungi (***Candida albicans, Candida parapsilosis, Candida glabrata*** and ***Candida tropicalis***). Filter paper disk (Whattman no.1) of 5 mm. diameter had been sterilized by autoclaving at 121°C for 15 min. Sterilized disks had been impregnated with (100µg/disk) of all evaluated compounds. The disks' surface inoculated by (100 µL) of both cultures of the tested microorganism. The impregnated disk had been incubated for 1 h. at 5°C to allow a well diffusion and then incubated for 24 h. at 37°C. The inhibition zones of evaluated compounds on the microorganisms were measured.

Total antioxidant capacity (Das et al., 2019)

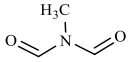
The total antioxidant capacity of the synthesized compounds was evaluated by the phosphomolybdenum method. A different concentrations (50, 100, 150 µg/mL) of an aliquot compound solutions was combined with (1 mL) of reagent ((0.6 M) sulfuric acid, (28 mM) sodium phosphate and (4 mM) ammonium molybdate). All test tubes containing the reaction solution for the tested compounds were capped and incubated at 95°C for 90 min. Then, the tubes were cooled to room temperature and then the absorbance of each tube was measured using a spectrophotometer at 695 nm against blank. The total antioxidant activity is expressed as the number of gram equivalent of ascorbic acid. Different concentrations (10, 20, 30, 50, 70, 90, 120, 180, 200 µg/mL) of ascorbic acid with DW where used to plot the calibration curve.

Results and Discussion:

The synthetic series for preparation of new five member heterocyclic rings comprising: Thiazolidin-4-one, Oxazolidin-5-one and Imidazolidine-4-one derivatives that produced from Schiff bases of 6-amino-1,3-dimethyluracil derivatives with different reagents via one-pot synthesis as showed in Scheme (1).



Scheme (1): Synthesis of new derivatives of Thiazolidin-4-one, Oxazolidin-5-one and Imidazolidine-4-one

Schiff bases derivatives (**1-6**) were synthesized via the nucleophilic addition reaction of 6-amino-1,3-dimethyluracil with a number of substituted aromatic aldehydes in absolute ethanol as solvent. The formation condensation mechanism (Al-Adhami and Al-Majidi, 2016) of Schiff bases derivatives (**1-6**) includes nucleophilic addition of amino group of 6-amino-1,3-dimethyluracil to carbonyl groups of different aromatic aldehydes(Al-Adhami and Al-Majidi, 2021) resulting in an intermediates which eliminate water molecule and form compounds (**1-6**). Physical properties of Schiff bases (**1-6**) were afforded different colours and yields listed in Table (1). The FTIR of compounds (**1-6**) includes the disappearance of ν(NH_2) absorption bands of 6-amino-1,3-dimethyluracil, while appearance of new bands of the formation of imine groups ν(C=N) at (1656-1645)cm^{-1}. In addition to presence of ν(C-H) aromatic bands at (3095-3006)cm^{-1}, ν(C=O) amide absorption bands at (1679-1668)cm^{-1} and ν(C=C) aromatic bands at (1610-1562)cm^{-1} spectrum. While compounds (**4, 5**) appearance absorption bands of ν(O-H) groups at (3332, 3357)cm^{-1} respectively, also compound (**6**) show ν(NO_2) absorption bands at (1514)cm^{-1} asym., (1344)cm^{-1} sym. All FTIR data of compounds (**1-6**) listed in the Table (1). ^{1}H-NMR spectrum of Schiff's base compound (**3**) showed the disappearance of singlet signal of (-N<u>H</u>$_2$) protons of 6-amino-1,3-dimethyluracil and appearance a singlet signal at δ=(3.07)ppm of (-C<u>H</u>$_3$) protons, a singlet signal at δ=(3.28)ppm for () protons, a singlet signal at δ=(4.71)ppm due to (=C<u>H</u>-) proton, a singlet signal at δ=(6.59)ppm for (N=C<u>H</u>-) protons and multi signals at δ=(6.78-7.95)ppm belonged to aromatic ring protons. ^{1}H-NMR spectral data of Schiff's base (**3**) showed in Table (5). ^{13}C-NMR spectral data of Schiff's base (**3**) are listed in Table (6). On the other hand, ^{1}H-NMR spectrum of Schiff's base (**5**) showed the disappearance of singlet signal of (-N<u>H</u>$_2$) protons of 6-amino-1,3-dimethyluracil and

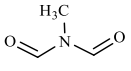
appearance a singlet signal at δ=(3.16)ppm of (-C<u>H</u>$_3$) protons, a singlet signal at δ=(3.48)ppm for () protons, a singlet signal at δ=(4.79)ppm due to (=C<u>H</u>-) proton, a singlet signal at δ=(6.54)ppm for (N=C<u>H</u>-) proton, multi signals at δ=(6.50-7.43)ppm belonged to aromatic ring protons and a singlet signal at δ=(9.92)ppm is due to (O-H) proton. ^{1}H-NMR spectral data of Schiff's base (**5**) showed in Table (5). ^{13}C-NMR spectral data of Schiff's base (**5**) are listed in Table (6).

Table 5- ^{1}H-NMR spectral data (δ ppm) for compounds (3,5,8,18,23&24)

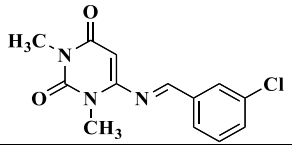
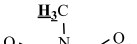
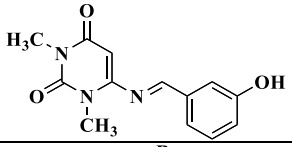
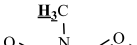
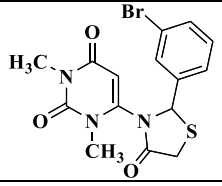
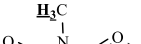
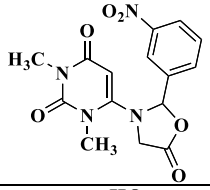
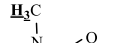
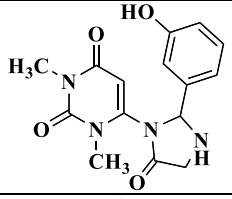
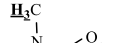
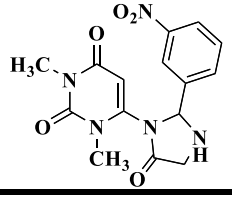
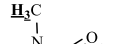
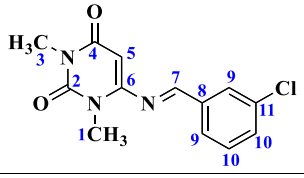
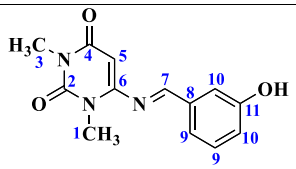
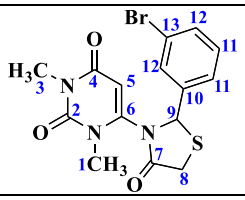
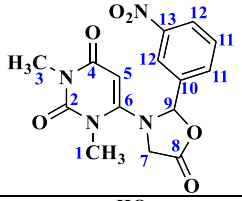
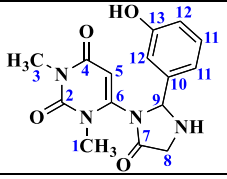
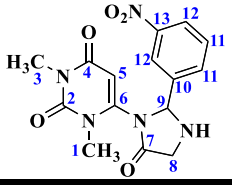
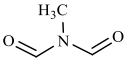
No.	Structures	^{1}HNMR Spectral data($^\delta$ppm)
3		3.07 (s, 3H, -C<u>H</u>$_3$); 3.28 (s, 3H, ); 4.71 (s, 1H, =C-<u>H</u>); 6.59 (s, 1H, N=C<u>H</u>-); 6.78-7.95 (m, 4H, Ar-<u>H</u>).
5		3.16 (s, 3H, -C<u>H</u>$_3$); 3.48 (s, 3H, ); 4.79 (s, 1H, =C-<u>H</u>); 6.54 (s, 1H, N=C<u>H</u>-); 6.50-7.43 (m, 4H, Ar-<u>H</u>); 9.92 (s, 1H, O-<u>H</u>).
8		3.08 (s, 3H, -C<u>H</u>$_3$); 3.28 (s, 3H, ); 3.75 (s, 2H, S-C<u>H</u>$_2$); 4.99 (s, 1H, N-C<u>H</u> thiazolidinone ring); 5.03(s, 1H, C=C-<u>H</u>); 6.76-7.73 (m, 4H, Ar-<u>H</u>).
18		3.02 (s, 3H, -C<u>H</u>$_3$); 3.17 (s, 3H, ); 3.85 (s, 2H, O=C-C<u>H</u>$_2$); 4.93 (s, 1H, N-C<u>H</u> oxazolidinone ring); 5.13(s, 1H, C=C-<u>H</u>); 6.85-7.46 (m, 4H, Ar-<u>H</u>).
23		3.01 (s, 3H, -C<u>H</u>$_3$); 3.15 (s, 3H, ); 3.59 (s, 2H, O=C-C<u>H</u>$_2$); 3.60 (s, 1H, N-C<u>H</u> imidazolidinone ring); 4.34 (s, 1H, C=C-<u>H</u>); 7.07-7.86 (m, 4H, Ar-<u>H</u>); 8.94 (s, 1H, -N-<u>H</u>); 10.01 (s, 1H, O-<u>H</u>).
24		3.01 (s, 3H, -C<u>H</u>$_3$); 3.16 (s, 3H, ); 3.61 (s, 2H, O=C-C<u>H</u>$_2$), (s, 1H, N-C<u>H</u> imidazolidinone ring); 4.41 (s, 1H, C=C-<u>H</u>); 6.48-7.43 (m, 4H, Ar-<u>H</u>); 8.91 (s, 1H, -N-<u>H</u>).

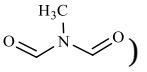
Table 6- ^{13}C-NMR spectral data (δ ppm) for compounds (3,5,8,18,23&24)

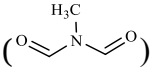
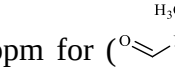
No.	Structures	^{13}C-NMR Spectral data($^\delta$ppm)
3		26.80 (**C$_1$**); 29.44 (**C$_3$**); 61.24 (**C$_7$**); 100.52 (**C$_5$**); 111.41 (**C$_9$**); 129.59 (**C$_8$**); 140.58 (**C$_{10}$**); 149.97 (**C$_6$**); 166.61 (**C$_2$**, **C$_4$**).

5		27.41 (**C_1**); 29.44 (**C_3**); 65.23 (**C_7**); 100.59 (**C_5**); 124.29 (**C_9**); 125.99 (**C_8**); 127.12 (**C_{10}**); 139.08 (**C_{11}**); 149.95 (**C_6**); 164.17 (**C_2**, **C_4**).
8		26.95 (**C_1**); 28.36 (**C_3**); 38.45 (**C_8**); 59.84 (**C_9**); 65.49 (**C_5**); 120.06 (**C_{11}**); 121.75 (**C_{13}**); 129.32 (**C_{12}**); 133.50 (**C_{10}**); 149.04 (**C_6**); 162.06 (**C_2**, **C_4**); 170.96 (**C_7**).
18		26.91 (**C_1**); 28.95 (**C_3**); 34.25 (**C_7**); 59.97 (**C_9**); 65.19 (**C_5**); 119.13 (**C_{11}**); 120.29 (**C_{13}**); 128.02 (**C_{12}**); 132.60 (**C_{10}**); 149.33 (**C_6**); 163.79 (**C_2**, **C_4**); 172.25 (**C_8**).
23		26.58 (**C_1**); 29.42 (**C_3**); 34.69 (**C_8**); 61.07 (**C_9**); 66.47 (**C_5**); 111.35 (**C_{11}**); 112.95 (**C_{13}**); 116.82 (**C_{12}**); 140.65 (**C_{10}**); 149.93 (**C_6**); 165.47 (**C_2**, **C_4**); 172.09 (**C_7**).
24		27.43 (**C_1**); 29.46 (**C_3**); 34.68 (**C_8**); 59.50 (**C_9**);65.03 (**C_5**); 124.43 (**C_{11}**); 125.85 (**C_{13}**); 128.90 (**C_{12}**); 132.11 (**C_{10}**); 149.91 (**C_6**); 165.22 (**C_2**, **C_4**); 171.99 (**C_7**).

The thiazolidin-4-one derivatives (**7-12**) were synthesized by the second cyclization method via one-pot synthesis of Schiff bases (**1-6**) with 2-mercaptoacetic acid in THF as a solvent as in Scheme (1). Physical properties of thiazolidin-4-one derivatives (**7-12**) are listed in Table (2) and FTIR spectra of these compounds were showed the disappearance of absorption bands of imine groups ν(C=N) at (1656-1645)cm^{-1}, while presence of absorption bands of ν(C-S) groups of thiazolidin-4-one rings at about (709-675)cm^{-1}. Besides these, appearance of ν(C-H) aromatic bands at (3097-3022)cm^{-1}, ν(C-H) aliphatic bands at (2977-2815)cm^{-1} and absorption bands of ν(C=O) amide groups overlap with ν(C=O) thiazolidin-4-one rings at (1701-1674)cm^{-1} and ν(C=C) aromatic bands at (1608-1558)cm^{-1}. The results are listed in Table (2). ^{1}H-NMR spectrum of compound (**8**) proved the disappearance of singlet signal of (N=C<u>H</u>-) of Schiff's base (**2**) and appearance a singlet signal at δ=(3.08)ppm of (-C<u>H</u>$_3$) protons, a singlet signal at δ=(3.28)ppm for () protons, a singlet signal at δ=(3.75)ppm of (S-C<u>H</u>$_2$) thiazolidin-4-one ring protons (Kumar et al., 2019), a singlet signal at δ=(4.99)ppm for (N-C-<u>H</u>) thiazolidin-4-one ring proton, a singlet signal at δ=(5.03)ppm due to (=C<u>H</u>-) proton and multi signals at δ=(6.76-7.73)ppm belonged to aromatic ring protons. ^{1}H-NMR spectral data of compound (**8**) showed in Table (5) and ^{13}C-NMR spectral data are listed in Table (6).

The third cyclization method of the synthesized oxazolidin-5-one derivatives (13-18) by one-pot reaction of Schiff bases (**1-6**) and chloroacetic acid with triethyl amine as a basic medium, as shown as Scheme (1). Some of the physical properties of oxazolidin-5-one derivatives (**13-18**) are listed in Table

(3). FTIR spectra of compounds (**13-18**) proved the disappearance of absorption bands of imine groups ν(C=N) at (1656-1645)cm^{-1}, while presence of absorption bands of ν(C-O) groups of oxazolidin-5-one rings at about (709-675)cm^{-1}. In addition of appearance of ν(C-H) aromatic bands at (3097-3053)cm^{-1}, ν(C-H) aliphatic bands at (2987-2821)cm^{-1}, ν(C=O) absorption bands of amide groups overlap with ν(C=O) of oxazolidin-5-one rings at (1693-1670)cm^{-1} and ν(C=C) aromatic bands at (1610-1583)cm^{-1}. The data results are illustrated in Table (3). ^{1}H-NMR spectrum of compound (**18**) proved the disappearance of singlet signal of (N=C<u>H</u>-) of compound (**18**) and appearance a singlet signal at δ=(3.02)ppm of (-C<u>H</u>$_3$) protons, a singlet signal at δ=(3.17)ppm for () protons, a singlet signal at δ=(3.85)ppm of (O=C-C<u>H</u>$_2$) oxazolidin-5-one ring protons, a singlet signal at δ=(4.93)ppm for (N-C-<u>H</u>) oxazolidin-5-one ring proton, a singlet signal at δ=(5.13)ppm due to (=C<u>H</u>-) proton and multi signals at δ=(6.85-7.46)ppm belonged to aromatic ring protons. ^{1}H-NMR spectral data of compound (**18**) illustrated in Table (5) while^{13}C-NMR spectral data in Table (6).

Schiff bases (**1-6**) cyclized by the fourth cyclization method using 2-aminoacetic acid in THF solvent to obtain imidazolidin-4-one derivatives (**19-24**) as in Scheme (1). Physical properties of imidazolidin-4-one derivatives (**19-24**) are illustrated in Table(4). FTIR spectra of compounds (**19-24**) showed the disappearance of absorption bands of imine groups ν(C=N) at (1656-1645)cm^{-1}, while appearance of ν(N-H) absorption bands of imidazolidin-4-one rings at (3388-3215)cm^{-1}. Also include appearance of ν(C-H) aromatic absorption bands at (3066-3053)cm^{-1}, ν(C-H) aliphatic bands at (2972-2825)cm^{-1}, ν(C=O) absorption bands of amide groups overlap with ν(C=O) of imidazolidin-4-one rings at (1731-1670)cm^{-1} and ν(C=C) aromatic bands at (1614-1585)cm^{-1}. The results are listed in Table (4). ^{1}H-NMR spectrum of compound (**23**) includes disappearance of singlet signal of (N=C<u>H</u>-) compoud (**5**) and appearance a singlet signal at δ=(3.01)ppm of (-C<u>H</u>$_3$) protons, a singlet signal at δ=(3.15)ppm for () protons, a singlet signal at δ=(3.59)ppm of (O=C-C<u>H</u>$_2$) imidazolidine-4-one ring protons, a singlet signal at δ=(3.60)ppm of (N-C<u>H</u>) imidazolidine-4-one ring proton, a singlet signal at δ=(4.34)ppm due to (=C<u>H</u>-) proton, multi signals at δ=(7.07-7.86)ppm belonged to aromatic ring protons, a singlet signal at δ=(8.94)ppm of (N-<u>H</u>) imidazolidine-4-one ring proton and a singlet signal at δ=(10.01)ppm due to (O-H) proton. ^{1}H-NMR spectral data of compound (**23**) illustrated in Table (5) and ^{13}C-NMR spectral data are illustrated in Table (6). ^{1}H-NMR spectrum of compound (**24**) proved the disappearance of singlet signal of (N=C<u>H</u>-) of compound (**6**) and appearance a singlet signal at δ=(3.01)ppm of (-C<u>H</u>$_3$) protons, a singlet signal at δ=(3.16)ppm for () protons, a singlet signal at δ=(3.61)ppm of (O=C-C<u>H</u>$_2$) imidazolidine-4-one ring protons, (N-C<u>H</u>) imidazolidine-4-one ring proton, a singlet signal at δ=(4.41)ppm due to (=C<u>H</u>-) proton, multi signals at δ=(6.48-7.43)ppm belonged to aromatic ring protons and a singlet signal at δ=(8.91)ppm of (N-<u>H</u>) Imidazolidine-4-one ring proton. ^{1}H-NMR spectral data of compound (**24**) illustrated in Table (5) while^{13}C-NMR spectral data in Table (6).

Biological activity

The biological activity the synthesized 6-amino-1,3-dimethyluracil derivatives had been evaluated on two Gram-positive bacteria (***Staphylococcus aureus*** and ***Staphylococcus epidermidis***)

and two Gram-negative bacteria (***Escherichia coli*** and ***Klebsiella pnemonia***). The antibacterial activity test results listed in the Table (7) showed that all tested compounds have no inhibition against (***Escherichia colia*** and ***Staphylococcus epidermidis***) expect compounds (**9** and **22**). While compound (**19**) have no inhibition against antibacterial activity(Al-Majidi and Al-Adhami, 2016). On the other hand, the rest tested compounds have weak or no inhibition against (***Klebsiella pneumonia*** and ***Staphylococcus aureus***). Compounds (**9** and **19**) have no inhibition against antifungal activity. While compound (**15**) have a strong and spesific inhibition zone against ***Candida parapsilosis*** but the rest of fungi had no inhibition as shown as Table (8).

Table 7- Antibacterial activity test of some prepared compounds

No.	*Escherichia coli*	*Klebsiella pnemonia*	*Staphylococcus aureus*	*Staphylococcus epidermidis*
3	-	-	9	-
5	-	-	9	-
6	-	-	10	-
8	-	10	-	-
9	11	8	-	-
11	-	-	10	-
15	-	8	10	-
19	-	-	10	8
19	-	-	-	-
21	-	-	8	-
22	8	-	9	-
Amoxicillin	-	33	32	33
control	-	-	-	-

[Control]: 100µg/ml; Solvent: dimethylsolfoxide
Inhibition Zone: (-) no inhibition; (6-10) weak; (11-18) moderate; (19-30) strong.

Table 8- Antifungal activity test of some prepared compounds

No.	*Candida albicans*	*Candida parapsilosis*	*Candida glabrata*	*Candida tropicalis*
10	-	-	-	-
15	-	12	-	-
19	-	-	-	-
Fluconazole	25	13	-	27
control	-	-	-	-

[Control]: 100µg/ml; Solvent: dimethylsolfoxide
Inhibition Zone: (-) no inhibition; (6-10) weak; (11-18) moderate; (19-30) strong.

Antioxidant activity

Generally, mechanism was used to study the antioxidant activity of the compounds, namely: total antioxidant capacity (TAOC)(Al-Adhami et al., 2020). All the synthesized compounds were generated *in vitro* by non-enzymatic system and determined spectrophotometrically by photo reduction method and the compounds were tested in five different concentrations.

In general, the phenolic compounds have been known to have antioxidant activities by their radical scavenging activities in addition of inducing antioxidant enzyme levels. Also, marine sources such as marine algae are rich in various antioxidant compounds(Al-Adhami et al., 2020).

Total antioxidant capacity: The total antioxidant capacity of all synthesized compounds (**1-24**) was evaluated according to the phosphomolybdenum method, which based on the reduction of colorless

Molybdenum(VI) to form blue Molybdenum(V) using the synthesized compounds and subsequent formation of a green phosphate - Mo(V) complex in acidic pH. The antioxidant activity of the compounds were compared to standard ascorbic acid. Among the newly synthesized uracil derivatives, compounds (**1-24**) possess weak antioxidant capacity against reduced Mo(VI) to Mo(V) as shown as Table (9).

Table 9- Evaluation of antioxidant capacity by phosphomolybdenum method

Comp. No.	50 µg/mL		100 µg/mL		150 µg/mL	
	Absorbance	Conc.	Absorbance	Conc.	Absorbance	Conc.
0.	0.02 ± 0.01	1.51	0.00± 0.02	3.03	0.00 ± 0.07	10.60
1.	0.00 ± 0.00	00.00	0.02 ± 0.02	3.03	0.01 ± 0.06	9.09
2.	0.00 ± 0.00	00.00	0.00 ± 0.00	00.00	0.00 ± 0.03	4.54
3.	0.00 ± 0.00	00.00	0.00± 0.01	1.51	0.00 ± 0.04	16.66
4.	0.00 ± 0.00	00.00	0.00 ± 0.02	3.03	0.06 ± 0.06	9.09
5.	0.00± 0.00	00.00	0.00 ± 0.00	00.00	0.00 ± 0.03	4.54
6.	0.00 ± 0.00	00.00	0.00 ± 0.01	1.51	0.00 ± 0.03	4.54
7.	0.00± 0.06	9.09	0.01 ± 0.10	15.15	0.02 ± 0.27	40.09
8.	0.02± 0.03	4.54	0.00 ± 0.02	3.03	0.07 ± 0.08	12.12
9.	0.00 ± 0.08	12.12	0.04± 0.04	6.06	0.01 ± 0.09	13.63
10.	0.00 ± 0.00	00.00	0.00 ± 0.00	00.00	0.01 ± 0.07	10.60
11.	0.00 ± 0.00	00.00	0.00 ± 0.00	00.00	0.00 ± 0.03	4.54
12.	0.00 ± 0.00	00.00	0.00 ± 0.02	3.03	0.03 ± 0.04	6.06
13.	0.01 ± 0.01	1.51	0.01± 0.03	4.54	0.02 ± 0.08	12.12
14.	0.00 ± 0.00	00.00	0.00 ± 0.02	3.03	0.01 ± 0.06	9.09
15.	0.00 ± 0.00	00.00	0.01 ± 0.03	4.54	0.01 ± 0.08	12.12
16.	0.02± 0.07	10.60	0.01 ± 0.08	12.12	0.02± 0.12	18.18
17.	0.00 ± 0.00	00.00	0.00 ± 0.00	00.00	0.01 ± 0.09	13.63
18.	0.01 ± 0.04	6.06	0.02 ± 0.08	12.12	0.00 ± 0.11	16.66
19.	0.03 ± 0.12	18.18	0.02± 0.07	10.60	0.02 ± 0.14	21.21
20.	0.00± 0.00	00.00	0.03 ± 0.09	13.63	0.02 ± 0.13	19.69
21.	0.00 ± 0.05	7.57	0.01 ± 0.18	27.27	0.05 ± 0.39	59.09
22.	0.00 ± 0.08	12.12	0.00 ± 0.10	15.15	0.00 ± 0.17	25.75
23.	0.00 ± 0.00	00.00	0.00 ± 0.00	00.00	0.01 ± 0.05	7.57
24.	0.01 ± 0.01	1.51	0.01 ± 0.05	7.57	0.02 ± 0.09	13.63
Standard	**0.07 ± 0.55**	**83.33**	**0.14± 1.09**	**165.15**	**0.03± 1.65**	**250.00**

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