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PHARMACOLOGICAL STUDIES ON DERIVATIVES OF CYTOSINE

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ABSTRACT: The Schiff bases of cytosine (I) 4-((2-hydroxy-3,5-diiodobenzylidene)amino) pyrimidin-2(1H)-one, (II) 4-((4-hydroxy-3-methoxybenzylidene) amino) pyrimidin-2(1H)-one, (III) 4-((3,4,5-trimethoxybenzylidene)amino) pyrimidin-2(1H)-one, (IV) 4-((furan-2-ylmethylene)amino) pyrimidin-2(1H)-one, (V) 4-((pyridin-4-ylmethylene)amino) pyrimidin-2(1H)-one, (VI) 4-((2-hydroxy-5-nitrobenzylidene)amino) pyrimidin-2(1H)-one, (VII) 4-((4-hydroxy-3-methoxy-5-nitrobenzylidene)amino) pyrimidin-2(1H)-one and (VIII) 4-((4-(diethylamino)-2-hydroxybenzylidene)amino) pyrimidin-2(1H)-one were prepared and characterized by physical and analytical data, FTIR , ^{1}H NMR, ^{13}C NMR spectra and were screened against gram positive bacteria Staphylococcus aureus, Basillussubtilis and gram negative bacteria Escherichia Coli, Klebsiellaaerogenes for antibacterial activity and were screened against Aspergillusniger and Candida albicans forantifungal activity by disc diffusion method. Ciprofloxacin and Nystatin were used as standard for bacteria and fungi.

Key words: **[**Cytosine,Staphylococcus aureus, Basillussubtilis, Escherichia Coli, Klebsiellaaerogenes, antifungal activity,Aspergillusniger, Candida albicans, Ciprofloxacin and Nystatin.]

1. INTRODUCTION

The findings of the Lancet study are shocking thatsuperbugs kill babies as antibiotic resistance rises. Nearly 25 percent of babies with sepsis died despite timely medical intervention and because of unresponsiveness to treatment, is worrisome. If 80 per cent of infection caused by acinetobacter and in more than 50 per cent of klebsiella infections, the first line treatment fails, it clearly indicates the rampant misuse of antibiotics. There is an indiscriminate use of antibiotics[1,2] and analgesic drugs.Unaffordable and inaccessible qualitative health-care services easy availability of drugs over the counter without any prescription and inadequate dosage recommendations by unqualified medical practitioners are the main reasons for the superbug menace. It would be major public health disaster if the rampant use of drugs were left unchecked.Recently[3-5]derivatives of cytosine were found to have potential non antibiotic resistance antibacterial, antiviral and anticancer properties. Our study clearly indicates on the antibacterial antifungal activities of derivatives of cytosine derived from condensation[6-11] of aldehyde and ketone with cytosine.

2. MATERIALS AND METHODS MATERIALS

All the reagents used were of AR grade. Commerciallyavailable rectified spirit was dried over anhydrousquicklime for 24 hours, filtered and distilled beforeuse (BP 78^{o}C). Dimethylsulphoxide (sigma) and N,Ndimethylformamide(sigma) were used as suchcytosine,

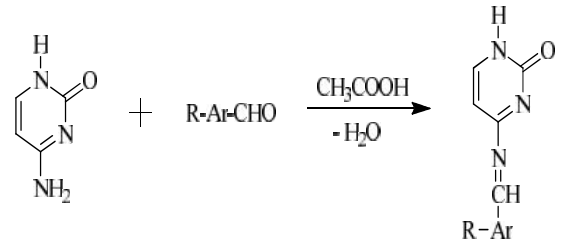
3,5-diiodosalicylaldehyde, vaniline, 34,5-trimethoxybenzaldehyde, furfural, pyridine-4-carboxaldehyde, 5-nitrosalicylaldehyde, 5-nitrovaniline and 4-diethylaminosalicylaldehyde were purchased from AlfaAesar.

Instruments

Melting points were determined using Elico melting point apparatus. Elemental analysiswereperformed using ElementarVario EL III. IR spectra of the compounds were recorded with KBrpellets with carry 630 FTIR Spectrometer in the 4000-400 cm-1range. The ^{1}HNMR and^{13}CNMRspectra were recorded on aBruker 400 MHz FT- PMR Spectrometer.

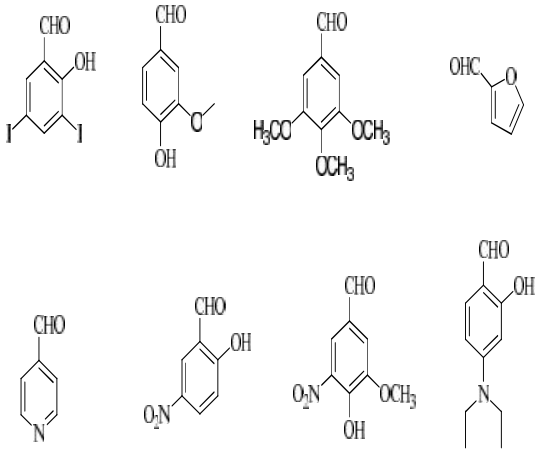
General preparation of derivatives of cytosine

All the azomethine compounds of derivatives of cytosine were prepared as reported in the literature[3-11]by the followingscheme – 1.



Scheme 1

Where, Ar-CHO =



Preparation of (I)4-((2-hydroxy-3,5-diiodobenzylidene)amino)pyrimidin-2(1H)-one To the hot solution of cytosine 1.11 g (0.01mol)in minimum amount of dimethyl formamideand the DMF solution of 3,5-diiodosalicylaldehyde 3.73 g (0.01mol) were mixed. Thereaction mixture was refluxed for 3 hrs. The yellowish-browncoloured solid mass 4-((2-hydroxy-3,5-diiodobenzylidene) amino) pyrimidin-2(1H)-one wasformed during refluxing. The crude product wascooled, filtered, washed with ethanol, ether and recrystallizedfrom DMF and then dried over vacuumdesiccator.

Preparation of (II)4-((4-hydroxy-3-methoxybenzylidene) amino) pyrimidin-2(1H)-one Cytosine (1.11 g, 0.01mol) was dissolvedin 5ml of hot glacial acetic acid,1.52 g (0.01mol) of vaniline was dissolved in 5ml of glacialacetic acid and were mixed. The reaction mixture wasrefluxed with stirring for 5 hours. The mixture was allowed to cool, and poured into ice. The crude solid4-((4-hydroxy-3-methoxybenzylidene)amino)pyrimidin-2(1H)-onewas

filtered off and washed withdistilled water, then re-crystallized from acetic acidand then dried over vacuum desiccator.

Preparation of (III)4-((3,4,5-trimethoxybenzylidene) amino) pyrimidin-2(1H)-one 25ml of ethanolic solution of cytosine(1.11 g, 0.01mol) was added to 25ml ofethanolicsolution of 3,4,5-trimethoxybenzaldehyde(1.96g, 0.01mol).Then three drops of glacial acetic acid was added to thereaction mixture. The reaction mixture was heated andrefluxed for about 5 hours at 90°C. The resultingsolution was further concentrated by water bath. Theproduct4-((3,4,5-trimethoxybenzylidene) amino) pyrimidin-2(1H)-one obtained wasprecipitated, cooled and collected after filtration. Theprecipitate was purified by washing with distilledwater and then with ethanol. The 4-((3,4,5-trimethoxybenzylidene) amino) pyrimidin-2(1H)-one was again recrystallized in ethanol and then dried overvacuum desiccator.

Preparation of (IV)4-((furan-2-ylmethylene)amino)pyrimidin-2(1H)-one

The 4-((furan-2-ylmethylene)amino)pyrimidin-2(1H)-one was prepared by stirring a methanolicsolution of cytosine (1.11 g, 0.01mol)with furfural (96 g, 0.01mol) in 1:1stoichiometric ratio at room temperature over 24hours.The precipitate obtained were filtered and washed withmethanol and recrystallized from methanol and thendried over vacuum desiccator.

Preparation of (V)4-((pyridin-4-ylmethylene)amino)pyrimidin-2(1H)-one

A mixture of Pyridine-4-carboxaldehyde 1.07 g (0.01mol) and cytosine 1.11 g (0.01mol) were grained witha pestle in an open mortar at room temperature for 3minutes. To this reaction mixture sulphuric acid 2dropsand 20ml DMF were added and grained for 5minutes. On completion of reaction as monitored byTLC, the light greenish-colored solid 4-((pyridin-4-ylmethylene)amino)pyrimidin-2(1H)-one was separated out. The obtained solid wasisolated by simple Buchner filtration and wasrecrystallized from DMF and then dried over vacuumdesiccator.

Preparation of (VI)4-((2-hydroxy-5-nitrobenzylidene)amino)pyrimidin-2(1H)-one 2.2 grams of cytosine (0.02mol) wasmixed with 3.3g of 5-nitrosalicylaldehyde (0.02mol)and was grained well in acidic acid medium at roomtemperature. The mixture was transferred into hundredmilliliter Round Bottom flask and was refluxed for sixhours in oil bath. The solid product 4-((2-hydroxy-5-nitrobenzylidene)amino)pyrimidin-2(1H)-onewasfiltered and washed with ethanol and recrystallized inDMSO and then dried over vacuum desiccator.

Preparation of (VII) 4-((4-hydroxy-3-methoxy-5-nitrobenzylidene) amino) pyrimidin-2(1H)-one

A mixture of 5-nitrovaniline (1.97 g,0.01mol)and cytosine (1.11 g, 0.01mol) wasgrained in a mortar with a pestle made of porcelain for10 minutes. The mixture turned pasty after fewminutes of grainding. It was grained till yellow colourproduct appears. The mixture was left overnight. Theresultant product 4-((4-hydroxy-3-methoxy-5-nitrobenzylidene)amino)pyrimidin-2(1H)-onewas recrystallized using ethanoland then dried over vacuum desiccator.

Preparation of (VIII) 4-((4-(diethylamino)-2-hydroxybenzylidene) amino) pyrimidin-2(1H)-one

4-((4-(diethylamino)-2-hydroxybenzylidene)amino)pyrimidin-2(1H)-one was prepared from equimolar quantity ofcytosine (1.11 g, 0.01mol) and 4-diethylaminosalicylaldehyde (1.93 g, 0.01mol) in 30 ml of methanolwere heated at 70^{o}C on water bath for 4-hrs inpresence of few drops of glacial acetic acid. The crudeproduct were obtained after removal of methanolunder reduced pressure. The products wererecrystallized from methanol and then dried overvacuum desiccator.

3. THE ANTIMICROBIAL SUSCEPTIBILITY PRINCIPLE

Disc impregnated with known concentration of**antibacterial** drug are placed on an agar plate that has been inoculated uniformly over the entire plate with a culture of the bacterium to be tested. The plate isincubated for 18 to 24 hours at 37^{o}C. During thisperiod, the **antibacterial** agent diffuses through the agar and may prevent the growth of the organism. Effectiveness of susceptibility is proportional to the diameter of the inhibition zone around the disc. Organisms which grow up to the edge of the disc are resistant.

4. PROCEDURE

The plate was labeled with the name of the culture,sample and standard at the bottom of the plate. Thensterile cotton swab on a wooden applicator stick was dipped into the bacterial suspension. Excess fluid was removed by rotating the swab and rubbed gently over the plate to obtain uniform distribution of theinoculums. The sterile disc was held on the inoculated plate with the help of micropipette. The sample was leveled in the sterile disc and incubated at 37^{o}C in an incubator. After incubation, the diameter of the zone of inhibition of growth was measured.

5. OBSERVATION REPORT

Inhibition zone > 15mm	**Highly active**
Inhibition zone > 10mm	**Moderatively active**
Inhibition zone > 5mm	**Slightly active**
Inhibition zone ≤ 5mm	**Inactive**

Table 1. OBSERVATION REPORT

6. RESULTS AND DISCUSSION

The physical and analytical data of (I) 4-((2-hydroxy-3,5-diiodobenzylidene)amino) pyrimidin-2 (1H)-one, (II) 4-((4-hydroxy-3-methoxybenzylidene)amino) pyrimidin-2 (1H)-one, (III) 4-((3,4,5-trimethoxybenzylidene)amino) pyrimidin-2 (1H)-one, (IV) 4-((furan-2-ylmethylene)amino) pyrimidin-2 (1H)-one, (V) 4-((pyridin-4-ylmethylene)amino) pyrimidin-2 (1H)-one, (VI) 4-((2-hydroxy-5-nitrobenzylidene)amino) pyrimidin-2 (1H)-one, (VII) 4-((4-hydroxy-3-methoxy-5-nitrobenzylidene)amino) pyrimidin-2 (1H)-one and (VIII) 4-((4-(diethylamino)-2-hydroxybenzylidene)amino) pyrimidin-2 (1H)-one are given in Table 2.

[I] 4-((2-hydroxy-3,5-diiodobenzylidene) amino) pyrimidin-2(1H)-one

FTIR (cm^{-1}): 3587 & 679 cm^{-1} ($-O-H$), 3285 & 650 cm^{-1} ($-\overset{|}{N}-H$), 1687 cm^{-1} ($>C=O$), 1633 cm^{-1} ($-N=\overset{|}{C}H$), 1624 cm^{-1} ($-N=\overset{|}{C}-$), 1210 cm^{-1} ($Ar-OH$) & 589 cm^{-1} ($Ar-I$)
^{1}HNMR δ (ppm): 8.48 (s, 1H), 8.43 (d, 1H), 8.07 (s, 1H), 8.00 (s, 1H), 7.88 (s, 1H), 5.40 (d, 1H) & 5.35 (s, 1H)
^{13}CNMR δ (ppm): 163.7 (s), 160.1 (s), 159.1 (s), 156.3 (s), 147.6 (s), 136.9 (s), 127.4 (s), 121.7 (s), 104.8 (s), 88.6 (s) & 83.8 (s)

[II] 4-((4-hydroxy-3-methoxybenzylidene) amino) pyrimidin-2(1H)-one

FTIR (cm^{-1}): 3606 & 690 cm^{-1} ($-O-H$), 3410 & 750 cm^{-1} ($-\overset{|}{N}-H$), 1710 cm^{-1} ($>C=O$), 1640 cm^{-1} ($-N=\overset{|}{C}H$), 1610 cm^{-1} ($-N=\overset{|}{C}-$), 1240 cm^{-1} ($-\overset{|}{N}-\overset{|}{C}<$), 1190 cm^{-1} ($Ar-OR$) & 1140 cm^{-1} ($ArO-R$)

^{1}HNMR δ (ppm): 8.48 (s, 1H), 8.43 (d, 1H), 8.00 (s, 1H), 7.52 (s, 1H), 7.34 (d, 1H), 6.91 (d, 1H), 5.40 (d, 1H), 5.35 (s, 1H) & 3.83 (s, 3H)

^{13}CNMR δ (ppm): 163.7 (s), 160.1 (s), 156.3 (s), 151.0 (s), 149.3 (s), 127.4 (s), 127.3 (s), 122.9 (s), 117.0 (s), 112.1 (s), 104.8 (s) & 56.1 (s)

[III] 4-((3,4,5-trimethoxybenzylidene) amino) pyrimidin-2(1H)-one FTIR (cm^{-1}): 3289 & 805 cm^{-1} (—N–H), 1732 cm^{-1} (>C=O), 1633 cm^{-1} (N=CH), 1606 cm^{-1} (—N=C—), 1237 cm^{-1} (Ar–OR) & 1120 cm^{-1} (ArO–R)

^{1}HNMR δ (ppm): 8.48 (s, 1H), 8.43 (d, 1H), 8.00 (s, 1H), 7.14 (s, 2H), 5.40 (d, 1H) & 3.83 (s, 9H)

^{13}CNMR δ (ppm): 163.7 (s), 160.1 (s), 156.3 (s), 153.2 (s), 141.5 (s), 128.0 (s), 127.4 (s), 104.8 (s), 104.0 (d), 60.8 (s) & 56.1 (s)

[IV] 4-((furan-2-ylmethylene) amino) pyrimidin-2(1H)-one

FTIR (cm^{-1}): 3270 & 750 cm^{-1} (—N–H), 1700 cm^{-1} (>C=O), 1640 cm^{-1} (—N=CH), 1620 cm^{-1} (—N=C—), 1230 cm^{-1} (ArO–R) & 1040 cm^{-1} (—N–C<)

^{1}HNMR δ (ppm): 8.43 (d, 1H), 8.00 (s, 1H), 7.75 (d, 1H), 7.50 (s, 1H), 6.93 (d, 1H), 6.52 (t, 1H) & 5.40 (d, 1H)

^{13}CNMR δ (ppm): 163.7 (s), 160.1 (s), 156.3 (s), 149.1 (s), 144.4 (s), 127.4 (s), 118.9 (s), 112.6 (s) & 104.8 (s)

[V] 4-((pyridin-4-ylmethylene) amino) pyrimidin-2(1H)-one

FTIR (cm^{-1}): 3300 & 770 cm^{-1} (—N–H), 1640 cm^{-1} (—N=CH), 1620 cm^{-1} (—N=C—) & 1110 cm^{-1} (—N–C<)

^{1}HNMR δ (ppm): 8.66 (d, 2H), 8.43 (s, 1H), 8.00 (s, 1H), 7.98 (d, 2H), 7.50 (s, 1H) & 5.40 (d, 1H)

^{13}CNMR δ (ppm): 163.7 (s), 160.1 (s), 156.3 (s), 149.4 (d), 144.3 (s), 127.4 (s), 120.4 (s) & 104.8 (s)

[VI] 4-((2-hydroxy-5-nitrobenzylidene) amino) pyrimidin-2(1H)-one

FTIR (cm^{-1}): 3622 & 778 cm^{-1} (—O–H), 3271 & 814 cm^{-1} (—N–H), 1741 cm^{-1} (>C=O), 1651 cm^{-1} (—N=CH), 1633 cm^{-1} (—N=C—) and 1480 cm^{-1} (Ar–NO$_2$)

^{1}HNMR δ (ppm): 8.48 (s, 1H), 8.43 (d, 1H), 8.35 (s, 1H), 8.05 (d, 1H), 8.00 (s, 1H), 7.28 (d, 1H), 5.40 (d, 1H) and 5.35 (s, 1H)

^{13}CNMR δ (ppm): 167.2 (s), 163.7 (s), 160.1 (s), 156.3 (s), 140.6 (s), 128.6 (s), 127.4 (s), 125.5 (s), 119.4 (s), 116.9 (s) and 104.8 (s)

[VII] 4-((4-hydroxy-3-methoxy-5-nitrobenzylidene) amino) pyrimidin-2(1H)-one

FTIR (cm^{-1}): 3280 & 796 cm^{-1} (—N–H), 3262 & 751 cm^{-1} (—O–H), 1741 cm^{-1} (>C=O), 1642 cm^{-1} (—N=CH), 1633 cm^{-1} (—N=C—), 1570 cm^{-1} (Ar–NO$_2$), 1309 cm^{-1} (Ar–OR) and 1246cm^{-1} (ArO–R)

^{1}HNMR δ (ppm): 8.48 (s, 1H), 8.43 (d, 1H), 8.00 (s, 1H), 7.91 (s, 2H), 5.40 (s, 1H), 5.35 (s, 1H) and 3.83 (s, 3H)

^{13}CNMR δ (ppm): 163.7 (s), 160.1 (s), 156.3 (s), 152.4 (s), 140.3 (s), 138.1 (s), 128.2 (s), 127.4 (s), 118.2 (s), 116.5 (s), 104.8 (s) and 56.1 (s)

[VIII] 4-((4-(diethylamino)-2-hydroxybenzylidene) amino) pyrimidin-2(1H)-one

FTIR (cm^{-1}): 3253 & 841 cm^{-1} (—N–H), 3145 & 688 cm^{-1} (—O–H), 3064 cm^{-1} (—C–C<), 1678 cm^{-1} (—N=CH), 1624 cm^{-1} (—N=C—) and 1237 cm^{-1} (Ar–N—)

^{1}HNMR δ (ppm): 8.48 (s, 1H), 8.43 (d, 1H), 8.00 (s, 1H), 7.48 (d, 1H), 6.37 (d, 1H), 6.30 (s, 1H), 5.40 (d, 1H), 3.41 (q, 4H) and 1.15 (t, 6H)

^{13}CNMR δ (ppm): 163.7 (s), 162.0 (s), 160.1 (s), 156.3 (s), 153.3 (s), 132.8 (s), 127.4 (s), 108.4 (s), 104.8 (s), 104.5 (s), 47.1 (d) and 12.9 (s)

Derivatives of Cytosine	Molecular Weight	Nature of Appearance	% of yield	Elemental Analysis (in %)				
				C	H	O	N	I
[I] $C_{11}H_7I_2N_3O_2$	467.00	Yellow Crystalline Solid	85	28.29	1.51	6.85	9.00	54.35
[II] $C_{12}H_{11}N_3O_3$	245.23	Yellow Crystalline Solid	87	58.77	4.52	19.57	17.13	-
[III] $C_{14}H_{15}N_3O_4$	289.28	Yellow Crystalline Solid	68	58.13	5.23	22.12	14.53	-
[IV] $C_9H_7N_3O_2$	189.17	Yellow Crystalline Solid	79	57.14	3.73	16.92	22.21	-
[V] $C_{10}H_8N_4O$	200.19	Yellow Crystalline Solid	80	59.99	4.03	7.99	27.99	-
[VI] $C_{11}H_8N_4O_4$	260.19	Yellow Crystalline Solid	84	50.77	3.10	24.60	21.53	-
[VII] $C_{12}H_{10}N_4O_5$	290.23	Yellow Crystalline Solid	86	49.66	3.47	27.56	19.30	-
[VIII] $C_{15}H_{18}N_4O_2$	286.329	Yellow Crystalline Solid	77	62.92	6.34	11.18	19.57	-

Table 2.The physical and analytical data of derivatives of cytosine

7. ANTIBACTERIAL BIOASSAY

Antibacterial activities [12, 13] of derivatives of cytosine were screened against bacterial gram positive bacteriaStaphylococcus aureus, and gram negative bacteria Escherichia coli, Klebsiellaaerogenesand Bacillussubtilisby disc diffusion method and the resul tsobtained were formulated in Table.3 and Fig. 1-4 The experiments were carried out in DMSO solution at a concentration of 100ppm using Muller Hinton agar media. Ciprofloxacin was used as astandard.

8. ANTIFUNGAL BIOASSAY

Antifungal[14,15] screening of derivatives of cytosine werecarried out against Aspergillusniger and Candidaalbicansby disc diffusion method and the resultsobtained were formulated in Table.3 and Fig. 5and 6. The test was carried out in DMSO solution at aconcentration of 100 ppm. Results were comparedwith Nystatin at the same concentration.

Table 3.Antibacterial and antifungal activity of derivatives of Cytosine

Compounds	Gram negative Bacterias		Gram positive Bacterias		Fungi	
	E. coli	K. aerogenes	B. subtilis	S. aureus	A. niger	C. albicans
I	32	26	36	33	31	29
II	31	25	35	31	29	28
III	33	25	34	29	27	27
IV	31	24	32	28	26	26
V	33	22	30	27	24	24
VI	26	20	27	25	23	20
VI	24	18	26	23	20	19
VII	20	17	23	22	17	18
VIII	18	15	21	19	15	17
S. control	-	-	-	-	-	-
Standard	38	30	40	35	35	32


Fig. 1

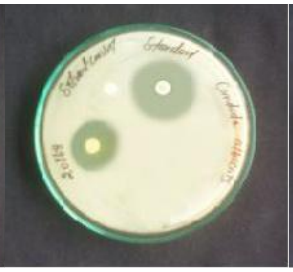


Fig. 2


Fig. 3


Fig. 4


Fig. 5


Fig. 6

The antibacterial and antifungal activity of azomethine compounds I- VIII (table. 3 and figure 1-6) clearly indicate that they inhibit the growth of tested bacteria and fungi in the decreasing order I>II>III>IV>V>VI>VII>VIII. Azomethine compounds I- VIII prevent bacterial reproduction by acting as an antimetabolite to paraamino benzoic acid (PABA), where PABA is a vital component in the biosynthesis of tetrahydrofolic acid. Competitive inhibition of PABA processing enzymes by I-VIII ultimately blocks the action of dihydrofolic acid synthetase, and therefore prevents dihydrofolic acid formation. As bacteria are unable to take up tetrahydrofolic acid from their surroundings, inhibition of dihydrofolic acid synthetase will starve the bacteria of thymidine and uridine. These two nucleosides are required for DNA replication and transcription, therefore cell growth and division is disrupted, and thus provides enough time for the body's own immune system to eliminate the bacterial threat [17].
The nature of bonding and structure of azomethineorganic compounds were elucidated [3-5] by the elementalanalysis, Melting Point, FTIR, ^{1}H NMR,^{13}C NMR, Chromatography and Molar ratio methods Gomathiet.al were prepared 4-(3-ethoxy-2-hydroxybenxzelideneaminno-N-(thiazole-2-yl-) benzene sulfonamide, Mohamed et.al and wereprepared 4-(-phenyl-propylideneamino)-benzene sulfonamide. In accordance with the dataobtained from antibacterial activities of 4-((2-hydroxy-3,5-diiodobenzylidene)amino) benzenesulfonamideand 4-((2-hydroxy-3,5-diiodobenzylidene)amino)-N-(thiazole-2-yl-) benzenesulfonamide, were moderatelyinhibited the growth of tested bacteria but ourderivatives of cytosine cytosine (I) 4-((2-hydroxy-3,5-diiodobenzylidene)amino) pyrimidin-2(1H)-one, (II) 4-((4-hydroxy-3-methoxybenzylidene)amino) pyrimidin-2(1H)-one, (III) 4-((3,4,5-trimethoxybenzylidene)amino) pyrimidin-2(1H)-one, (IV) 4-((furan-2-ylmethylene)amino) pyrimidin-2(1H)-one, (V) 4-((pyridin-4-ylmethylene)amino)pyrimidin-2(1H)-one, (VI) 4-((2-hydroxy-5-nitrobenzylidene)amino)pyrimidin-2(1H)-one, (VII) 4-((4-hydroxy-3-methoxy-5-nitrobenzylidene)amino) pyrimidin-2(1H)-one and (VIII) 4-((4-(diethylamino)-2-hydroxybenzylidene)amino)pyrimidin-2(1H)-one were highly inhibited the growthof tested bacteria.
In accordance with the data obtained from antifungalactivities of 4-(3-ethoxy-2-hydroxybenxzelideneamino-N-(thiazole-2-yl-)benzenesulfonamide[16](Gomathi et.al)were moderately inhibited the growth of tested fungibut our derivatives of cytosine (I) 4-((2-hydroxy-3,5-diiodobenzylidene)amino) pyrimidin-2(1H)-one, (II) 4-((4-hydroxy-3-methoxybenzylidene)amino) pyrimidin-2(1H)-one, (III) 4-((3,4,5-trimethoxybenzylidene)amino) pyrimidin-2(1H)-one, (IV) 4-((furan-2-ylmethylene)amino) pyrimidin-2(1H)-one, (V) 4-((pyridin-4-ylmethylene)amino) pyrimidin-2(1H)-one, (VI) 4-((2-hydroxy-5-nitrobenzylidene)amino) pyrimidin-2(1H)-one, (VII) 4-((4-hydroxy-3-

methoxy-5-nitrobenzylidene)amino) pyrimidin-2(1H)-one and (VIII) 4-((4-(diethylamino)-2-hydroxybenzylidene)amino) pyrimidin-2(1H)-one were highly inhibited thegrowth of tested fungi.From the results and previous work, antibacterial andantifungal activity studies were indicated that iodinesubstituted derivatives of cytosine were moreactive against bacteria and fungi than other derivativesof cytosine.

CONCLUSION

The derivatives of cytosine (I) 4-((2-hydroxy-3,5-diiodobenzylidene) amino) pyrimidin-2(1H)-one, (II) 4-((4-hydroxy-3-methoxybenzylidene) amino) pyrimidin-2(1H)-one, (III) 4-((3,4,5-trimethoxybenzylidene) amino) pyrimidin-2(1H)-one, (IV) 4-((furan-2-ylmethylene) amino) pyrimidin-2(1H)-one, (V) 4-((pyridin-4-ylmethylene) amino) pyrimidin-2(1H)-one, (VI) 4-((2-hydroxy-5-nitrobenzylidene) amino) pyrimidin-2(1H)-one, (VII) 4-((4-hydroxy-3-methoxy-5-nitrobenzylidene) amino) pyrimidin-2(1H)-one and (VIII) 4-((4-(diethylamino)-2-hydroxybenzylidene) amino) pyrimidin-2(1H)-one were prepared andbio-assay were tested against important bacteria and fungi.It was shown that the growth of bacteria and fungiwere highly inhibited by the derivatives of cytosine.

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