

## DESIGN, SYNTHESIS, CHARACTERIZATION OF NEW PYRIMIDINES DERIVED FROM CHALCONES AND STUDIES THEIR ANTIMICROBIAL ACTIVITIES

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### ABSTRACT

Many new 2,4,6-substituted pyrimidines namely 4(substituted)phenyl-6-(*p*-chlorophenyl or *p*-nitrophenyl)-2-oxo(1H)pyrimidines, 4(substituted)phenyl-6-(*p*-chlorophenyl or *p*-nitrophenyl)-2-imino(1H)pyrimidines and 4(substituted)phenyl-6-(*p*-chlorophenyl or *p*-nitrophenyl)-2-thioxo(1H)-pyrimidines, with substituents *p*-benzenesulphonamido, *p*-uriedo, *p*(4',N-methylaminophenyl)azo were synthesized. All synthesised pyrimidines were characterized by its melting points FTIR, <sup>1</sup>HNMR, and <sup>13</sup>C NMR and Mass spectral analysis.

Antimicrobial activities of all synthesised pyrimidines were examined against Gram-Ve (*Serratia marcescens*, *pseudomonas aeruginosa*), G+Ve bacteria (*Staphylococcus aureus* and *streptococcus pyogenes*) and (*candida albicans*) fungi in comparism with Cephalexin, Amoxicillin, and Tetracycline, Lincomycin pharmaceutical antibioticis, Nystatine and Flucanazole antifungal treatments.

Results showed good antibacterial effect, much better than antibiotics used in these studies, specially that pyrimidines containing imino and thioxo in postions-2. All synthesised pyrimidines showed very good inhibition effect against *candida albicans* fungi, specially that pyrimidines containing N-methylphenylazophenyl group at position-4.

**KEYWORDS:** Pyrimidines, Antimicrobial Activity

### INTRODUCTION

Pyrimidine is the most important member of all the diazine as this heterocyclic ring system occurs widely in living organisms. Purine, uric acid, alkoxan, barbituric acid, and also in agricultural chemical, as succuful treatment of various diseases<sup>[1-3]</sup>.

Pyrimidines have a long and distinguished history extending from the days of their discovery as an important constituent of nucleic acids to their current use in the chemotherapy of AIDS. During the last two decades, several pyrimidines derivatives have been developed as chemotherapeutic agents and have found wide clinical applications. Many pyrimidines and related heterocyclic compounds are found to possess a wide important pharmacophore and privileged structure in medicinal chemistry<sup>[4]</sup>.

Pyrimidines and their derivatives are considered to be important for drugs and agricultural chemicals. The use of pyrimidines is critical to successful treatment of various diseases. Pyrimidine derivatives possess several interesting biological activities such as antimicrobial, antitumour, antifungal, anticancer, antiviral, antibacterial, antioxidant, antiallergic, antidepressant, antitubercular, anti-HIV-1, antineoplastic, antimalarial, anti-Inflammatory, analgesic,

dopamine D<sub>3</sub>-receptor antagonist's activity, and herpes inhibiting activity, adenosine receptor antagonists and dihydrofolate reductase inhibitors<sup>[5-21]</sup>. Many pyrimidine derivatives are used for thyroid drugs and leukaemia. Although there are numerous classes of drugs that are routinely used to treat the diseases in humans, there are major four subcategories that contain pyrimidine base structure like Barbiturates and Nitropyrimidines<sup>[22,23]</sup>.

## EXPERIMENTAL

### Materials

All the chemicals were supplied by BDH and Fluka and used without further purification.

### Measurement

Melting point of compounds was measured with an electrothermal Stuart melting point apparatus.

Infrared spectra were recorded using (8300) (FTIR) shimadzu spectrophotometer in the range (4000- 400) cm<sup>-1</sup>, as (KBr discs).

H NMR and <sup>13</sup>C NMR spectra were carried out by: Ultra shield 300 MHZ, Bruker, Switzerland at University of Al- Albayt (in Jordan), and are reported in ppm, DMSO -d<sub>6</sub> was used as solvent with TMS as an internal standard.

The Mass spectra recorded on Varian Saturn 2000 GC-MS-MS system, electron impact (EI) or chemical ionisation (CI) modes, Molecular mass, range 45- 650 Dalton, at Institute of Organic and Pharmaceutical Chemistry (IOPC), National Hellenic Research Foundation, Athens, Greece.

Antimicrobial activity are examined against Gram-Ve bacteria (*Serratia marcescens*, *Pseudomonas aeruginosa*) and Gram+Ve bacterial (*Staphylococcus aureus*, *Streptococcus pyogenes*), were spread on Muller- Hinton agar plates using sterile cotton swabs. At a concentration (4 mg/mol). The antifungal activity (*Candida albicans*) using Sabouraud Dextrose agar plates using sterile cotton swabs. At a concentration (4 mg/ml). DMSO used as a solvent. The antimicrobial activity was performed in Ibn Al-Haitham Advisory office, the central service laboratory, University of Baghdad.

## PREPARATION OF 1, 3 SUBSTITUTED CHALCONES

Chalcones namely [1(*p*-benzenesulphonamido)phenyl-3-(*p*-chlorophenyl or *p*-nitrophenyl)-2-propene-1-one, A and B]; [1(*p*-ureido)phenyl-3(*p*-chlorophenyl or *p*-nitrophenyl)-2-propene-1one, C and D]; [1-*p*(4',N-methylaminophenyl)-*p*-azophenyl-3(*p*-chlorophenyl or *p*-nitrophenyl)-2-propene-1-one, E and F]; and [1(*p*-amino)phenyl-3(*p*-chlorophenyl or *p*-nitrophenyl)-2-propene-1-one; G and H], were prepared according to Reference[24].

## B. PREPARATION OF 2, 4, 6 SUBSTITUTED PYRIMIDINE

### Preparation of [4(substituted)phenyl-6-(*p*-chlorophenyl or *p*-nitrophenyl)-2-oxo(1H)pyrimidines [1,2,7,8,13,14,19 and 20]

A mixture of any of following chalcones A to H (0.5mmol), urea (0.06g, 1mmol) and sodium hydroxide (0.04g, 1mmol), were dissolved in absolute ethyl alcohol (30ml). Reaction mixture was refluxed for (24 hrs.), then cooled and poured into stirred ice-cold water, where a precipitated 2-oxopyrimidine was formed, filtered and washed with water then dried. Recrystallized from chloroform: petroleum ether (b.p. 60-80°C). Physical properties of prepared 2-oxopyrimidine are given in Table (1).

### Preparation of [4(substituted)phenyl-6-(*p*-chlorophenyl or *p*-nitrophenyl)-2-imino(1H)pyrimidines [3,4,9,10,15,16,21 and 22]

A mixture of any of following chalcones A to H (0.5mmol), quinidine hydrochloride (0.095g, 1mmol) and sodium hydroxide (0.08g, 2mmol), were dissolved in absolute ethyl alcohol (30ml). Reaction mixture was refluxed for (24 hrs.), then cooled and poured into a stirred ice-cold water, where a precipitated 2-iminopyrimidine was formed, filtered and washed with water then dried. Recrystallized from methyl alcohol: petroleum ether (b.p. 60-80°C). Physical properties of prepared 2-iminopyrimidine are given in Table (1).

### Preparation of [4(substituted)phenyl-6-(*p*-chlorophenyl or *p*-nitrophenyl)-2-thioxo(1H)pyrimidines [5,6,11,12,17,18,23 and 24]

A mixture of following chalcones A to H (0.5mmol), thiourea (0.07g, 1mmol) and sodium hydroxide (0.04g, 1mmol), were dissolved in absolute ethyl alcohol (30ml). Reaction mixture was refluxed for (24 hrs.), then cooled and poured into a stirred ice-cold water, where a precipitated 2-thioxopyrimidine was formed, filtered and washed with water, then dried. Recrystallized from methyl alcohol:benzene. Physical properties of prepared 2-thioxopyrimidine are given in Table (1).

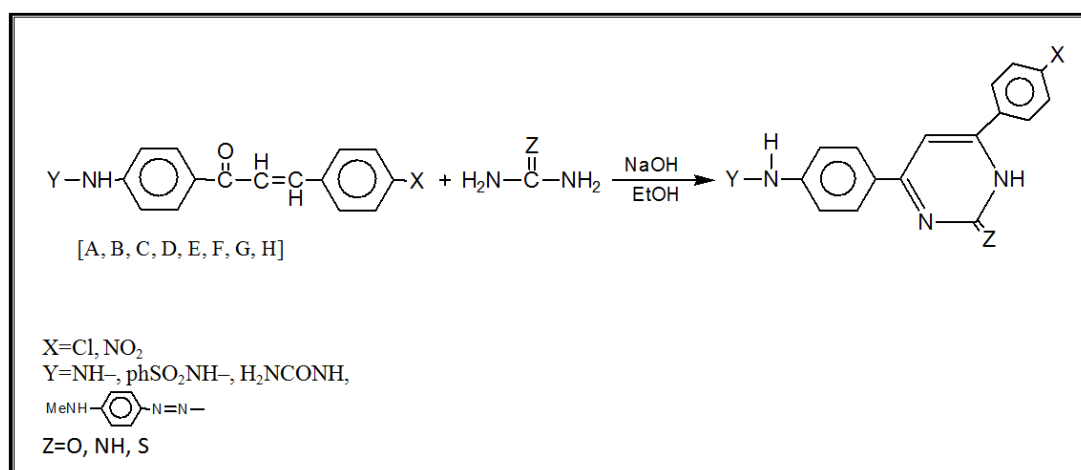


Figure 1

## RESULT AND DISCUSSIONS

Because of the importance of pyrimidine derivative in the field of pharmaceutical treatments as an active antimicrobial compounds, we design to synthesis three types 2-pyrimidine namely-2-oxo-pyrimidine, 2-iminopyrimidine and 2-thioxopyrimidine, having substituent at position 4 and 6, like *p*-chlorophenyl or *p*-nitrophenyl at position-4, and *p*(benzenesulphonamido)phenyl, *p*-uriedophenyl, 4[*p*(4',N-methylaminophenyl)azo]phenyl and *p*-aminophenyl, via condensation of synthesized chalcones [1(*p*-substituted)phenyl-3(*p*-chlorophenyl or *p*-nitrophenyl)-2-propene-1-one,A-H]<sup>[24]</sup>, with *p*-benzenesulphonamidophenyl, *p*-uriedophenyl, 4[*p*(4',N-methylaminophenyl)azo]phenyl and *p*-aminophenyl substituent at position-1, with urea, quinidine hydrochloride and thiourea respectively.

## Synthesis of [4(*p*-substituted) phenyl-6-(*p*-chlorophenyl or *p*-nitrophenyl)-2-oxo (1H) pyrimidines] [1, 2, 7, 8, 13, 14, 19 and 20]

These types of synthesized pyrimidines, characterized by FTIR,  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR and Mass spectral analysis.

IR- spectrums of [1 and 2] pyrimidines, showed sulphonamido ( $\text{SO}_2\text{NH}$ -) bands (Amide II and I) as well as to (NH and C=O) carbamido ( $-\text{HN}-\text{C}=\text{O}$ ), ethylenic ( $\text{CH}=\text{C}$ ) and (C=N) stretching bands of pyrimidine ring, and asymmetrical/ symmetrical ( $\text{NO}_2$ ) stretching bands of pyrimidine [2]. All these bands are summarized in Table (2).

$^1\text{H}$  NMR- spectral analysis of pyrimidine [1], showed sulphonamido (NH) and carbamido (NH), ethylenic ( $\text{CH}=\text{C}$ ) as singlet signal protons, beside aromatic (13H) multiple signal protons. While  $^{13}\text{C}$  NMR spectrum of this pyrimidine showed carbamido (C=O), ethylenic ( $\text{CH}=\text{C}$ ) and (C=N) carbon signals of pyrimidine ring and aromatic carbon multiple signals. All these signals are summarized in Tables (3) and (4) respectively. Mass spectral analysis of this pyrimidine showed ( $\text{M}+\text{H}$ )<sup>+</sup> ion at  $m/z$  (438).

IR- spectral analysis of pyrimidines [7 and 8] showed, ( $\text{NH}_2$ ) asymmetrical/ symmetrical and (NH) of uriedo ( $\text{NH}_2\text{CONH}$ ) with (NH) of carbamido (NHCO) of pyrimidine ring beside to (C=O) of uriedo and carbamido, ( $\text{CH}=\text{C}$ ) ethylenic and (C=N) groups of pyrimidine ring stretching bands, also asymmetrical/ symmetrical ( $\text{NO}_2$ ) stretching bands of pyrimidine [8]. All these bands are given in Table (2).

$^1\text{H}$  NMR- spectrum of pyrimidine [7], showed uriedo ( $\text{NH}_2$  and NH), carbamido (NH), ethylenic ( $\text{CH}=\text{C}$ ) as singlet signal protons, beside a two aromatic ring (8H) as a multiple signal protons. While  $^{13}\text{C}$  NMR spectrum of this pyrimidine, showed uriedo and carbamido (C=O) carbon signals beside to ethylenic ( $\text{CH}=\text{C}$ ), (C=N) of pyrimidine ring and aromatic rings carbon signals. All these signals are summarized in Tables (3) and (4) respectively.

Pyrimidines [13 and 14], IR- spectral analysis showed, amino (NH), carbamido (NH) and (C=O), ethylenic ( $\text{CH}=\text{C}$ ), (C=N) of pyrimidine stretching bands as well as to azo ( $\text{N}=\text{N}$ ) stretching band, also asymmetrical/ symmetrical ( $\text{NO}_2$ ) stretching bands of pyrimidine [14]. All these bands are given in Table (2).

$^1\text{H}$  NMR- spectrum of pyrimidine [13] showed, amino (NH and  $\text{NCH}_3$ ), carbamido (NH) of pyrimidine as singlet signals protons, beside to ethylenic ( $\text{CH}=\text{C}$ ) pyrimidine and (12H) aromatic protons as a multiplet signals. While  $^{13}\text{C}$  NMR of this pyrimidine showed, amino ( $\text{N}-\text{CH}_3$ ), carbamido (C=O) of pyrimidine ring carbon signals beside to ethylenic ( $\text{CH}=\text{C}$ ), (C=N) pyrimidine ring and aromatic carbons as multiple signals. All these signals are given in Tables (3) and (4) respectively.

Pyrimidines [19 and 20], IR- spectrums showed, amino ( $\text{NH}_2$ ) asymmetrical/ symmetrical stretching bands beside to carbamido (NH and C=O), ethylenic ( $\text{CH}=\text{C}$ ), (C=N) pyrimidine stretching bands and also asymmetrical/ symmetrical ( $\text{NO}_2$ ) stretching bands of pyrimidine [20]. All these bands are given in Table (2).

$^1\text{H}$  NMR- spectrum of pyrimidine [19], showed amino ( $\text{NH}_2$ ) and carbamido (NH) as singlet signal protons, beside to ethylenic ( $\text{CH}=\text{C}$ ) and aromatic (8H) as multiplet signals. While  $^{13}\text{C}$  NMR-spectrum of this pyrimidine showed, carbamide (C=O) carbon signal and ethylenic ( $\text{CH}=\text{C}$ ), (C=N) of pyrimidine ring and aromatic carbons as multiple signals. All these signals are given in Tables (3) and (4) respectively [25,26,27].

**Synthesis of [4(substituted) phenyl-6-(*p*-chlorophenyl or *p*-nitrophenyl)-2-imino (1H) pyrimidines] [3, 4, 9, 10, 15, 16, 21 and 22]**

These types of synthesized pyrimidines characterized by FTIR, <sup>1</sup>H NMR, <sup>13</sup>C NMR and Mass spectral analysis.

IR- spectral analysis of pyrimidines [3 and 4] showed, sulphonamido (SO<sub>2</sub>NH) bands (Amide II and I) beside to (NH) and (C=N) of imidino (HN=C–NH) and pyrimidine ring, with ethylenic (CH=C) of pyrimidine ring stretching bands, also asymmetrical/ symmetrical (NO<sub>2</sub>) stretching bands of pyrimidine [4]. All these bands are summarized in Table (2).

Pyrimidine [3] <sup>1</sup>H NMR- spectrum showed, (NH) of sulphonamido, imidino, pyrimidine ring and ethylenic (CH=C) as singlet signals protons, beside aromatic (13H) as multiplet signal. While <sup>13</sup>C NMR spectrum of this pyrimidine showed, imidino (HN=C–NH), pyrimidine ring (C=N) and ethylenic (CH=C) carbon signals with aromatic carbon signals of phenyl rings. All these signals are summarized in Tables (3) and (4) respectively. Mass spectral analysis of this pyrimidine showed (M+H)<sup>+</sup> ion at m/z (437).

Pyrimidines [9 and 10], IR- spectrum showed, uriedo asymmetrical/ symmetrical (NH<sub>2</sub>) and uriedo, imidino and pyrimidine ring (NH) stretching bands, beside to uriedo (C=O), ethylenic (CH=C), imidino and pyrimidine ring (C=N) stretching bands, also asymmetrical/ symmetrical stretching bands of (NO<sub>2</sub>) for pyrimidine [10]. All these bands are summarized in Table (2).

<sup>1</sup>H NMR- spectrum for pyrimidine [9] showed, ethylenic (CH=C) and (NH) of pyrimidine ring, imidino (HN=C–NH) and uriedo (O=C–NH) protons as a singlet signals, as well as to (NH<sub>2</sub>) uriedo and (8H) aromatic protons as multiplet signals. While <sup>13</sup>C NMR-spectrum of this pyrimidine showed uriedo, imidino carbon signals beside to ethylenic (CH=C), (C=N) pyrimidine ring and aromatic carbons as multiplet signals. All these signals are summarized in Tables (3) and (4) respectively.

Pyrimidines [15 and 16], IR- spectral analysis showed, (NH) of amino, imidino pyrimidine ring (HN=C–NH) and imidino (HN=C), ethylenic (CH=C), pyrimidine ring (C=N) stretching bands, beside azo (N=N) stretching band, also asymmetrical/ symmetrical (NO<sub>2</sub>) stretching bands of pyrimidine [16]. All these bands are summarized in Table (2).

Pyrimidines [15], <sup>1</sup>H NMR- spectrum showed, amino (NH and NCH<sub>3</sub>) and pyrimidine ring (NH) as a singlet signal protons, beside imidino (HN=C), ethylenic (CH=C) and aromatic (12H) protons as multiple signals. While <sup>13</sup>C NMR of this pyrimidine showed (NCH<sub>3</sub>), imidino (–C=NH) of pyrimidine ring carbon signals, as well as to ethylenic (CH=C), (C=N) of pyrimidine ring and aromatic carbons as multiplet signals. All these signals are summarized in Tables (3) and (4) respectively.

IR- spectral analysis of [21 and 22] pyrimidines showed, asymmetrical/ symmetrical amino (NH<sub>2</sub>), (NH) of imidino (HN=C–NH) and pyrimidine ring stretching bands beside to ethylenic (CH=C), (C=N) of pyrimidine ring and imidino (C=NH) stretching bands, also asymmetrical/ symmetrical (NO<sub>2</sub>) for pyrimidine [22]. All these bands are summarized in Table (2).

<sup>1</sup>H NMR- spectral analysis for pyrimidine [21] showed, amino (NH<sub>2</sub>), imidino (HN=C–NH) as singlet signals protons, with ethylenic (CH=C), pyrimidine ring (NH) and (8H) aromatic as a multiplet protons. But <sup>13</sup>C NMR-spectrum of this pyrimidine showed, imidino (HN=C) carbon signals, with multiplet of ethylenic (CH=C), pyrimidine (N=C) and aromatic carbon signals, All these signals are summarized in Tables (3) and (4) respectively [25, 26, 27].

**Synthesis of [4(substituted) phenyl-6-(*p*-chlorophenyl or *p*-nitrophenyl)-2-thioxo (1H) pyrimidines] [5, 6, 11, 12, 17, 18, 23 and 24]**

These types of synthesized pyrimidines characterized by FTIR, <sup>1</sup>H NMR, <sup>13</sup>C NMR and Mass spectral analysis.

Pyrimidines [5 and 6], IR- spectrums showed, (NH) of thiocarbamido (S=C–NH) pyrimidine ring and sulphonamido (SO<sub>2</sub>NH) (Amide II and I) stretching bands, (C=S) thiocarbamido, ethylenic (CH=C) and (C=N) of pyrimidine ring stretching bands, also asymmetrical/ symmetrical stretching bands of (NO<sub>2</sub>) for pyrimidine [6]. All these bands are given in Table (2).

<sup>1</sup>H NMR - spectrum for pyrimidine [5] showed, (NH) sulphonamido and thiocarbamido with ethylenic (CH=C) of pyrimidine ring as singlet signals protons beside aromatic (13H) multiplet protons. While <sup>13</sup>C NMR-spectrum of this pyrimidine showed, thiocarbamido carbon signal, beside multiple signals ethylenic (CH=C), (C=N) of pyrimidine ring carbon signals with aromatic carbon signals. These entire signals are given in Table (3) and (4) respectively. Mass spectrum of pyrimidine [5] showed (M+H)<sup>+</sup> ion at m/z (454).

Pyrimidines [11 and 12], IR- spectral analysis showed, (NH<sub>2</sub>) asymmetrical/ symmetrical with (NH) of uriedo (NH<sub>2</sub>CONH), and thiocarbamido (SC–NH) pyrimidine ring stretching bands, beside to(C=O) uriedo, (C=S) thiocarbamido and ethylenic (CH=C), (C=N) of pyrimidine ring stretching bands. Also asymmetrical/ symmetrical stretching bands of (NO<sub>2</sub>) for pyrimidine [12]. All these bands are given in Tables (2).

<sup>1</sup>H NMR- spectrum for pyrimidine [11] showed, ethylenic (CH=C) and uriedo (NH) as a singlet signals protons, beside uriedo (NH<sub>2</sub>), thiocarbamido (NH) and aromatic (8H) as a multiplet signals protons. While <sup>13</sup>C NMR-spectrum of this pyrimidine showed, uriedo (C=O), thiocarbamido (C=S) of pyrimidine ring carbon signals, beside ethylenic (CH=C), (C=N) pyrimidine ring and aromatic carbons as multiplet signals. All these signals are given in Tables (3) and (4) respectively.

Pyrimidines [17 and 18], IR- spectrums showed, amino (NH), thiocarbamido (NH) and (C=S), ethylemic (CH=C) and (C=N) of pyrimidine ring, beside to azo (N=N) stretching bands, also asymmetrical/ symmetrical stretching bands of (NO<sub>2</sub>) for pyrimidine [18]. All these bands are given in Table (2).

<sup>1</sup>H NMR- spectrum of pyrimidine [17] showed, amino (NH and NCH<sub>3</sub>) and thiocarbamido (NH) of pyrimidine ring as singlet signals protons, but ethylenic (CH=C) of pyrimidine ring and aromatic (12H) as a multiplet signal protons. While <sup>13</sup>C NMR-spectrum of this pyrimidine showed, amino (N–CH<sub>3</sub>) and thiocarbamido (SC–NH) carbon signals, beside ethylenic (CH=C) of pyrimidine ring and aromatic as multiplet carbon signals. All these signals are given in Tables (3) and (4) respectively.

Pyrimidine [23 and 24] IR- Spectral analysis showed, amino (NH<sub>2</sub>) asymmetrical/ symmetrical with thiocarbamido (NH) of pyrimidine ring stretching band, beside ethylenic (CH=C), (C=N) of pyrimidine ring and thiocarbamido (C=S) stretching bands, also asymmetrical/ symmetrical (NO<sub>2</sub>) stretching bands of pyrimidine [24]. All these bands are given in Table (2).

<sup>1</sup>H NMR- spectrum of pyrimidine [23] showed, (NH<sub>2</sub>) amino singlet signal, beside ethylenic (CH=C), thiocarbamido (NH) of pyrimidine ring and aromatic (8H), as multiple signals protons. But <sup>13</sup>C NMR-spectrum of this pyrimidine showed, thiocarbamido (S=C–NH), (C=N) of pyrimidine ring carbon signals beside ethylenic (CH=C) of

pyrimidine ring and aromatic carbons multiple signals. All these signals are summarized in Tables (3) and (4) respectively [25, 26, 27].

## ANTIMICROBIAL ACTIVIT

Many pyrimidine derivatives have antimicrobial activities against some types of bacteria and fungi<sup>[4,8,28,29]</sup>. So, for this purposes, we design to synthesis some certain pyrimidine containing active antimicrobial group at positions-2, 4, 6 in order to improve its antimicrobial activities, like *p*-benzenesulphonamidophenyl, *p*-ureidophenyl and 4[*p*(4',N-methylaminophenyl)azo]phenyl groups at position-4, *p*-chloro or *p*-nitro phenyl group at postion-6 and oxo, imino and thioxo groups at position-2. Table (5), showed antimicrobial activities data of some synthesized pyrimidines [1–24] against some of (G-Ve and G+ve) bacteria like (*Serratia marcescens*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Streptococcus pyogenes*) respectively and (*Candida albicans*) fungi, in comparison with antimicrobial activities of some pharmaceutical antibiotics Cephalexin, Amoxicillin, Tetracycline and Lincomycin and antifungal Nystatine and Fluconazole treatments.

### Antimicrobial Data as in Table (5) Showed

**First:** pyrimidine contain benzenesulphonamido group [1 to 6] have much better effect than used antibiotics in this studies, on both type of (G-Ve) bacteria, specially that pyrimidines group containing imino [3 and 4] and thioxo groups [8 and 9] at positon-2.

**Second:** pyrimidine containing ureido group [7 to 12] have better effect than used antibiotic on both (G+Ve) *Staphylococcus aureus* and (G-Ve) *Serratia marcescens* and *Pseudomonas aeruginosa*, specially that pyrimidines containg imino group [9 and 10] and thioxo group [11] at positon-2.

**Third:** pyrimidines containing 4[*p*(4',N-methylaminophenyl)azo]phenyl group [13 to 18] have strong inhibition effect more than used antibiotics in this study, on both types of (G-Ve and G+Ve) bacteria (*Serratia marcescens*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Streptococcus pyogenes*) respectively, specially that pyrimidines containing imino group [15 and 16], thioxo group [17 and 18] at position-2.

**Fourth:** While pyrimidines containing amino group [19 to 24], showed also better effect than used antibiotic in this study, on both (G+Ve) *Staphylococcus aureus* and (G-Ve) *Serratia marcescens*, *Pseudomonas aeruginosa*, specially that pyrimidine containg imino group [21 and 22] and thioxo group [23 and 24] at position-2.

**Fifth:** Also all synthesized pyrimidines [1 to 24] showed good effect on (*Candida albicans*) fungi, in comparison with pharmaceutical antifungal treatment specially that pyrimidine [13], containg 4[*p*(4',N-methylaminophenyl)azo]phenyl group at position-4 and oxo group at position- 2, showed strong effect more than antifungal Nystatine treatments.

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## APPENDICES

**Table 1: Physical Properties for Compounds Series One**

No.	Name of compound	M.wt	m.p	Wight of product	Yield %	Colour
(1)	[4-(p-benzenesulphonamidophenyl)- 6-p-chlorophenyl-2-oxo-pyrimidine]	438.5	164-167	0.12	54	Pale-Yellow
(2)	[4-(p-benzenesulphonamidophenyl)- 6-p-nitrophenyl-2-oxopyrimidine]	449	150-153	0.10	44	Brown
(3)	[4-(p-benzenesulphonamidophenyl)-6-p-chlorophenyl-2-iminopyrimidine]	434.5	190-198	0.10	46	Yellow
(4)	[4-(p-benzenesulphonamidophenyl)-6-p-nitrophenyl-2-imino pyrimidine]	448	146-148	0.14	62	orange
(5)	[4-(p-benzenesulphonamido) phenyl-6-p-chlorophenyl-2-thioxo pyrimidine]	454.5	140-143	0.20	88	Yellow
(6)	[4-(p-benzenesulphonamido)phenyl-6-p-nitrophenyl-2-thioxo pyrimidine]	465	130-134	0.15	64	Orange
(7)	[4(p-Ureido-phenyl)-6-p-chloro-phenyl-2-oxo-1H-pyrimidine]	341.5	135-138	0.10	58	Light-orange
(8)	[4(p-Ureido-phenyl)-6-p-nitro-phenyl-2-oxo-1H- pyrimidine]	352	150-153	0.096	54	brown
(9)	[4(p-Ureido-phenyl)-6-p-chloro-phenyl-2-imino-1H-pyrimidine]	340.5	156-159	0.13	76	yellow
(10)	[4(p-Ureido-phenyl)-6-p-nitro-phenyl-2-imino-1H-pyrimidine]	351	162-164	0.09	51	Brown
(11)	[4(p-Ureido-phenyl)-6-p-chloro-phenyl-2-thioxo-1H-pyrimidine]	357.5	145-147	0.10	55	yellow
(12)	[4(p-Ureido-phenyl)-6-p-nitro-phenyl-2-thioxo-1H- pyrimidine]	368	165-168	0.07	38	orange
(13)	4[p(4',N-methylaminophenyl)azo]phenyl-6-chlorophenyl-2-oxo, 1H pyrimidine	416.5	212-215	0.14	67	Pale-brown
(14)	4[p(4',N-methylaminophenyl) azo]phenyl-6-nitrophenyl-2-oxo,1H pyrimidine	427	206-209	0.12	56	Dark-brown
(15)	4[p(4',N-methylaminophenyl)azo]phenyl-6-chlorophenyl-2-imino, 1H pyrimidine	415	204-206	0.16	77	Pale-brown
(16)	4[p(4',N-methylaminophenyl)azo]phenyl-6-nitrophenyl-2-imino,1H pyrimidine	426	160-163	0.091	42	orange
(17)	4[p(4',N-methylaminophenyl)azo]phenyl)-6-chlorophenyl-2-thioxo, pyrimidine]	432.5	193-196	0.15	69	brown
(18)	4[p(4',N-methylaminophenyl)azo]phenyl-6-nitrophenyl-2-thioxo, 1H pyrimidine	443	155-158	0.08	36	Dark-brawn
(19)	[4(p-aminophenyl)-6-p-chloro-phenyl-2-oxo-1H pyrimidine]	298.5	127-130	0.05	33	orange
(20)	[4(p-aminophenyl)-6-p-nitro-phenyl-2-oxo-1H pyrimidine]	309	154-157	0.07	45	Dark-brown

**Table 1: Condt**

(21)	[4(p-aminophenyl)-6-p-chloro-phenyl-2-imino-1H pyrimidine]	297.5	180-182	0.08	53	Light-orange
(22)	[4(p-aminophenyl)-6-p-nitro-phenyl-2-imino-1H pyrimidine]	308	170-173	0.066	42	yellow
(23)	[4(p-aminophenyl)-6-p-chloro- phenyl-2-thioxo-1H pyrimidine]	314.5	170-174	0.072	45	Pale-orange
(24)	[4(p-aminophenyl)-6-p-nitro-phenyl-2-thioxo-1H pyrimidine]	325	156-158	0.06	37	brown

Table 2: FT-IR Spectral Data (Wave Number  $\nu$ ) for Pyrimidines [1–24]

Comp. No.	$\nu$ (-NH <sub>2</sub> ) & (-NH)	$\nu$ (CH=C) & (C=N)	$\nu$ (SO <sub>2</sub> -NH) Amide II & I	$\nu$ (C=O) Carbamido ring and uriedo	$\nu$ (-C=NH) Imidino	$\nu$ (C=S) Thio-carbamido	$\nu$ (N=N) azo	$\nu$ (-NO <sub>2</sub> )
[1]	3410 3255	1604	1330 1161	1654	-	-	-	-
[2]	3154 3116	1600	1342 1161	1658	-	-	-	1516 1342
[3]	3340 3278 3201	1604	1334 1161	-	1604	-	-	-
[4]	3491 3390 3290	1604	1346 1161	-	1604	-	-	1516 1396
[5]	3360 3248	1604	1330 1161	-	-	1230	-	-
[6]	3476 3384	1604	1338 1161	-	-	1222	-	1516 1336
[7]	3471 3433 3367 3217	1593	-	1678	-	-	-	-
[8]	3480 3410 3250 3150	1593	-	1681	-	-	-	1519 1346
[9]	3468 3340 3336 3197	1589	-	1662	1598	-	-	-
[10]	3425 3367 3313 3201	1635	-	1670	1635	-	-	1531 1350
[11]	3450 3340 3197	1585	-	1678	-	1234	-	-
[12]	3464 3371 3201	1577	-	1678	-	1234	-	1527 1334
[13]	3479 3429 3380	1597	-	1651	-	-	1492	-

[14]	3471 3410 3340	1597	–	1651	–	–	1500	1519 1342
[15]	3487 3402 3244	1597	–	–	1597	–	1492	–
[16]	3591 3402 3209	1600	–	–	1600	–	1500	1535 1346
[17]	3440 3433 3155	1597	–	–	–	1157	1492	–
[18]	3367 3217 3136	1573	–	–	–	1238	1500	1527 1334
[19]	3460 3344 3221	1519	–	1597	–	–	–	–
[20]	3464 3363 3228	1600	–	1697	–	–	–	1516 1338
[21]	3464 3367 3221	1593	–	–	1593	–	–	–
[22]	3471 3356 3205	1570	–	–	1570	–	–	1531 1363
[23]	3440 3363 3217	1593	–	–	–	1234	–	–
[24]	3444 3352 3217	1566	–	–	–	1234	–	1512 1334

Table 3: <sup>1</sup>H-NMR Spectral Data (δPpm) for Pyrimidines

Comp. No.	SO <sub>2</sub> -NH sulphon-amido	NH <sub>2</sub> uriedo	-NH ureido	-NH amino	-N-CH <sub>3</sub> amino	-NH <sub>2</sub> amine	CH=C Ethylene	Aromatic-H	NH ring	C=NH imidino
[1]	10.9	–	–	–	–	–	7.2	7.3–7.7	8.1	–
[3]	11.0	–	–	–	–	–	7.2	7.4–7.9	7.7	8.1
[5]	10.4	–	–	–	–	–	7.1	7.3–7.8	8.1	–
[7]	–	7.9	9.0	–	–	–	6.1	7.1–7.8	6.5	–
[9]	–	7.5	8.8	–	–	–	5.9	7.6–8.2	6.6	7.3
[11]	–	7.2	8.8	–	–	–	6.0	7.3–8.4	7.0	–
[13]	–	–	–	3.4	3.7	–	7.2–8.0	7.2–8.0	6.6	–
[15]	–	–	–	3.6	3.8	–	6.6–7.8	6.6–7.8	6.7	6.6–7.8
[17]	–	–	–	3.5	3.7	–	7.2–8.6	7.2–8.6	6.7	–
[19]	–	–	–	–	–	6.6	7.2–8.1	7.2–8.1	7.2–8.1	–
[21]	–	–	–	–	–	6.5	7.3–8.2	7.3–8.2	7.3–8.2	6.7
[23]	–	–	–	–	–	6.7	7.2–8.7	7.2–8.7	7.2–8.7	–

Table 4:  $^{13}\text{C}$ -NMR Spectral Data ( $\delta\text{Ppm}$ ) for Pyrimidines

Comp. No.	C=O uriedo	-N-CH <sub>3</sub>	C=O carbamido	C=NH imidino	C=S Thiocarbamido	CH=C, C=N And Aromatic-C
[1]	–	–	185	–	–	117–141
[3]	–	–	–	152	–	118–141
[5]	–	–	–	–	175	118–145
[7]	163	–	187	–	–	117–147
[9]	163	–	–	148	–	119–144
[11]	156	–	–	–	187	114–147
[13]	–	33	185	–	–	117–155
[15]	–	33	–	162	–	117–152
[17]	–	33	–	–	177	117–144
[19]	–	–	185	–	–	111–154
[21]	–	–	–	154	–	111–132
[23]	–	–	–	–	195	111–154

Table 5: Antimicrobial Activity of Compounds [1– 24]

Comp. No.	Mean of Inhibition zone Diameter (mm)				
	<i>Staphylococcus aureus</i>	<i>Streptococcus pyogenes</i>	<i>Serratia marcescens</i>	<i>Pseudomonas aeruginosa</i>	<i>Candida albicans</i>
[1]	–	–	16	–	15
[2]	–	–	–	17	–
[3]	15	–	21	13	–
[4]	–	–	20	12	–
[5]	–	–	18	15	–
[6]	15	–	19	–	13
[7]	12	–	18	17	13
[8]	17	–	–	16	8
[9]	15	–	–	18	14
[10]	–	–	–	13	14
[11]	–	–	–	16	12
[12]	–	–	–	–	12
[13]	11	–	20	13	Large inhibition zone
[14]	–	–	19	18	14
[15]	24	20	12	23	13
[16]	26	38	28	19	12
[17]	35	35	25	25	10
[18]	38	24	–	26	14
[19]	15	–	19	11	12
[20]	15	–	17	11	12
[21]	17	–	19	12	13
[22]	–	17	15	18	–
[23]	–	–	17	11	11
[24]	11	–	16	18	12
Cephalexin	–	–	13	–	–
Amoxicillin	–	12	–	–	–
Tetracycline	25	25	–	12	–
Lincomycine	17	30	–	21	–
Nystatine	–	–	–	–	29
Fluconazole	–	–	–	–	–
Dimethyl-sulphoxide	–	–	–	–	–