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Synthesis, Identification and Antimicrobial Activity of 2-Phenyl-3-(Ethyl Acetate)-Quinazolin-4(3h)-One Nucleus Linked with Pyrazole, Pyrazolinone and Pyrimidine Ring

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Abstract--*A new series of pyrazole, pyrazolinone and pyrimidine derivatives were synthesized from quinazolin-4(3H)-one nucleus and then their actions as antimicrobial agents estimated in present work. Quinazolinone skeleton as starting compound was designed in three steps. The first step including formation of 2-benzamidobenzoic acid [1] by reaction of anthranilic acid with benzoyl chloride. The second step produced 2-phenyl-4H-benzo[3,1]oxazin-4-one [2] from cyclized of compound [1] by acetic anhydride. The third step involved gave 2-phenyl-3-(ethyl acetate)-quinazolin-4(3H)-one [3] by treatment of compound [2] with ethyl glycinate. Compound [3] was reacted with paraphenylenediamine to give 2-phenyl-3-(acetamido-4-aminophenyl)-quinazolin-4(3H)-one [4]. The diazotization of compound [4] with sodium nitrate and concentration HCl at 0-5 ^{o}C form diazonium salt that coupled with active methylene compounds such as acetyl acetone and ethyl aceto acetate to afforded corresponding compounds [5] and [6]. Hydrazono acetyl acetone [5] and hydrazono ethyl aceto acetate [6] treatment with hydrazine and substituted hydrazine to yielded series of pyrazole derivatives [7-11] and pyrazolinone derivatives [12-16] respectively. pyrimidine derivatives [17-18] prepared* ***via*** *cyclization of hydrazono acetyl acetone [5] with urea and thiourea. The newly synthesized compounds elucidate their structure by different spectral techniques involved FTIR, ^{1}H-NMR and ^{13}C-NMR. Some of its physical properties were measured. Furthermore we have evaluated the activity of some prepared compounds against different types of bacteria and fungi strain. The result showed significant effects for these compounds on microorganisms.*

Key words*--Quinazolin-4(3H)-one , Pyrazole , Pyrazolinone , Pyrimidine , Anti-microbial*

I. INTRODUCTION

Nitrogen-containing heterocyclic compounds are well-known skeletons in a variety of synthetic drugs, bioactive natural products pharmaceuticals, agrochemicals and pharmaceutical industry in medicinal chemistry [(1)]. Food and drug administration databases (FDA) in USA reveals the important of nitrogen-based heterocycles in the drug design, because nearly 60% of drug molecules containing a nitrogen heterocycle [(2)].

Quinazolinones are widely distributed in several families of plant kingdom as well as in microorganisms and animal [(3)]. Quinazolinone derivatives constitute an important class of fused heterocyclic due it occurrence in more than approximately 200 naturally occurring isolated alkaloids [(4)]. As therapeutics

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many of quinazolinones display anthelmintic [5], antimalarial [6], antimicrobial [7], antiviral [8], insecticidal [9], antihistaminic[10], antidepressant and anticonvulsant [11], activities.

Pyrazole a hetero aromatic ring involve of two nitrogen atoms at adjacent position [12]. The formation of pyrazole and its derivatives including the reaction of hydrazone with alkynes [13] or reaction of α,β-unsaturated aldehydes / ketones with hydrazine salts [14]. This ring found in different categories of biologically active molecules with various applications such as anti-alzheimer, anticancer, antihypercholesterolemic, antihyperglycemic, antihypertensive, antileishmanial, antimicrobial, antiparkinsonian, antipsychotic, neuroprotective [15].

Pyrimidine is six membered aromatic ring consist of carbon with two nitrogen atoms [16]. Because of wide occurrence for pyrimidine nucleus in nucleic acids, vitamins, coenzymes and nucleotides in addition alkaloids gained from tea, coffee, cocoa and in uric acid led to the Pyrimidine containing compounds play pivotal roles in biological processes of pharmaceutical, also agrochemical research and material sciences [17].

In recent years, attention in the chemistry of N-containing heterocyclic compounds increasing due to their biological significance, so this work is undertaken to finding a new suitable derivative from quinazolinone, which would exceed its activity the action of known market drugs containing the same ring.

Experimental Chemicals and Characterization techniqes.

All chemicals and solvents were supplied by sigma Aldrich,Merck, Fluka, and BDH company without further purification. Melting points were recorded by using open-ended capillary tube on Gallena kamp electro-thermal melting point apparatus (variable heater), England. FTIR were recorded by using Shimadzu (8400s) fourier transform infrared spectrometer, Japan, KBr disk (4000-600) cm^{-1}. Department of chemistry, college of Science, University of Baghdad, Iraq.^{1}H- NMR and^{13}C-NMR recorded by using Bruker (500,600) MH_Z, DMSO-d_6 and $CDCl_3$ as solvent, TMS used as internal standard. Sharif University of Technology, Iran. The antimicrobial activity was performed by Central Service laboratory, College of Education for pure science (Ibn Al-haitham), University of Baghdad.

Synthesis of 2-benzamidobenzoic acid [1] [18].

To cold and stirred solution of anthranilic acid (1.37g, 0.01mol) dissolved in (5mL) dry acetone , benzoyl chloride (1.16mL, 0.01mol) with (0.5mL) dry pyridine was added dropwise with kept cooling by using ice bath, the mixture was refluxed for (3hours) in water bath at (50-60)^{o}C, then poured into cold (5%HCl). The solid pale yellow precipitate was filtered, washed with distilled water, dried and recrystallized from ethanol-water. Physical properties and FTIR spectral data were listed in table (1).

Synthesis of 2-phenyl-4H-benzo[3,1]oxazin-4-one [2] [19].

In round bottom flask (2g, 0.008mol) of compound [1] dissolved in acetic anhydride (1.5mL, 0.016mol) was refluxed for (4hours). The solution cooled to room temperature then poured into cold petroleum ether to formed crystals that recrystallized from ethanol. Physical properties and FTIR spectral data were listed in table (1).

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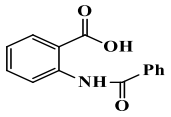
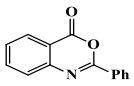
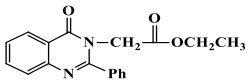
Synthesis of 2-phenyl-3-(ethylacetate)-quinazolin-4(3H)-one [3] [(20)].

To (1g, 0.004mol) of compound [2] in (3mL) dry DMF, ethyl glycinate (0.5g, 0.004mol) dissolved in (1mL) dry DMF was added in presence of dry pyridine (0.5mL), then refluxed for (4hours). The reaction mixture was poured into cold (5%HCl), solid precipitate was obtained filtered, washed with distilled water, dried and recrystallized from ethanol. Physical properties and FTIR spectral data were listed in table (1).

Table 1: Physical properties and FTIR spectral data cm^{-1} of compounds (1-3)

Com. No.	structure	Physical properties			FTIR absorption cm^{-1}			
		M.P. ^{O}C	Yield %	Color	ν(N-H)	ν(C=O)	ν(C=N)	Others
1		160- 162	75	Pale yellow	3240	1710 acid 1685 amide	——	ν(OH) 3436
2		110-112	85	Off white	——	1764 lactone	1643	ν(C-H) aromatic 3056
3		96- 98	80	Pale orange	——	1739 ester 1683 amide	1643	ν(C-H) aliphatic 2989 2902

Synthesis of 2-phenyl-3-[2-acetamido-4-amino phenyl]-quinazolin-4(3H)-one [4] [(21)].

Sodium carbonate (0.212g, 0.002mol) was added to (0.72g, 0.002mol) of compound [3] dissolved in (10mL) absolute ethanol, the mixture was stirred and added to solution of (0.216g, 0.002mol) p-phenylene diamine dissolved in (10mL) absolute ethanol. Final mixture refluxed for (10hours), then cooled to room temperature and poured into ice-cold distilled water to give solid crystalline precipitate that filtered , dried and recrystallized from ethanol-water. Physical properties and FTIR spectral data were listed in table (2).

Synthesis of 2-phenyl -3-[2-acetamido-4-phenyl-2-hydrazono-(2,4-dioxopentan-3-ylidene)]-quinazolin-4(3H)-one [5] and 2-phenyl -3-[2-acetamido-4-phenyl-2-hydrazono-(ethyl-3-oxo-butanoate)]-quinazolin-4(3H)-one [6] [(22)].

Gradually addition with vigorous stirring of cold solution contained (0.056g, 0.0008mol) sodium nitrate dissolved in (5mL) water to the cold solution of compound [4] (0.3g, 0.0008mol) dissolved in (2mL) concentrated HCl. The mixture was cooled in ice bath at 0-5^{o}C and stirred for (30minute). This cold condition must be maintaining for all reaction time. Then the diazonium mixture added slowly to solution of acetyl acetone (0.0008mol) or ethyl acetoacetate (0.0008mol), sodium acetate (0.064g, 0.0008mol) dissolved in (5mL) ethanol absolute with continuous stirring for (30minute). The precipitate was filtered, washed with distilled

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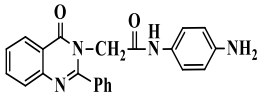
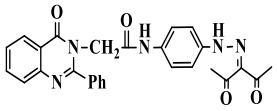
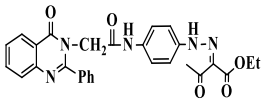
water and recrystallized from convenient solvent. Physical properties and FTIR spectral data were listed in table (2).

Table 2: Physical properties and FTIR spectral data cm^{-1} of compounds (4-6)

Com. No.	structure	Physical properties			FTIR absorption cm^{-1}			
		M.P. ^{O}C	Yield %	Color	ν(N-H)	ν(C=O)	ν(C=N)	Others
4		153-155	91	Gray	3315	1687 amide	1643	$\nu(NH_2)$ asym.3469 sym.3421
5		148-149	88	Pale yellow	3431 3400	1724 ketone 1676 amide	1648	ν(C=C) 1600 1533
6		169-170	82	Off white	3429	1735 ester 1716 ketone 1672 amide	1633	ν(C=C) 1608 1591

Synthesis of 2-phenyl-3-[2-acetamido-4-phenyl-diazenyl-(1-substitutedphenyl-3,5-dimethyl-1H-pyrazol-4-yl)]-quinazolin-4(3H)-one [7-11] and 2-phenyl -3-[2-acetamido-4-phenyl-2-hydrazinyl-(3-methyl-5-oxo-1-substitutedphenyl-1H-pyrazol-4(5H)-ylidene)]-quinazolin-4(3H) -one [12-16] [(23)].

Hydrazine hydrate and its derivatives (0.0006mol) dissolved in (10mL) absolute ethanol was added with continuous stirring to (0.3g, 0.0006mol) of compound [5] or [6] dissolved in (10mL) absolute ethanol. The reaction mixture was refluxed for (12-14) hours and cooled by poured in chilled water. The solid precipitate was filtered and recrystallized from convenient solvent. Physical properties and FTIR spectral data were listed in table (3) and (4).

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Table 3 Physical properties and FTIR spectral data cm^{-1} of compounds (7-11)

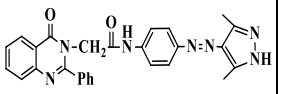
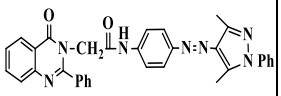
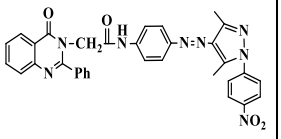
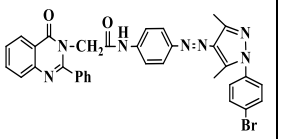
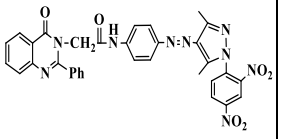
Com. No.	structure	Physical properties			FTIR absorption cm^{-1}			
		M.P. ^{o}C	Yield %	Color	ν(N-H)	ν(C=O)	ν(C=N)	Others
7		166-167	81	White	3317	1694 quinaz. 1679 amide	1654	ν(N=N) 1448
8		179-181	77	Light yellow	3247	1689 quinaz. 1677 amide	1636	ν(N=N) 1446
9		222-223	69	Brown	3253	1696 quinaz. 1680 amide	1649	ν(NO_2) asy.1539 sym.1369 ν(N=N) 1450
10		152-154	83	Pale brown	3247	1694 quinaz. 1678 amide	1653	ν(N=N) 1444 ν(C-Br) 671
11		287-289	75	Shine orange	3325	1692 quinaz. 1669 amide	1624	ν(NO_2) asy.1527 sym.1371 ν(N=N) 1448

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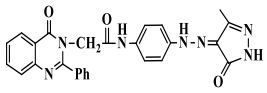
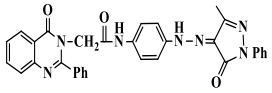
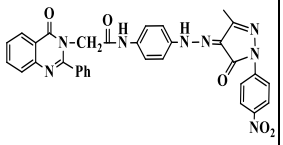
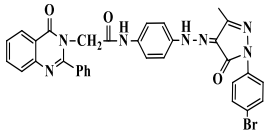
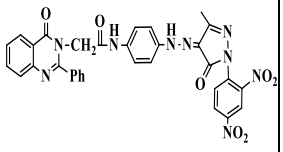
Table 4 Physical properties and FTIR spectral data cm^{-1} of compounds (12-16)

Com. No.	structure	Physical properties			FTIR absorption cm^{-1}			
		M.P. ^{O}C	Yield %	Color	ν(N-H)	ν(C=O)	ν(C=N)	Others
12		177-178	87	White	3309	1700 pyrazo. 1688 quinaz. 1664 amide	1635	ν(C=C) arom. 1600 1529
13		160-162	69	Light yellow	3238	1702 pyrazo. 1690 quinaz. 1662 amide	1638	ν(C=C) arom. 1602 1521
14		153-154	78	Dark brown	3261	1703 pyrazo. 1685 quinaz. 1670 amide	1648	$\nu(NO_2)$ asy.1519 sym.1342
15		200-202	82	Shine brown	3259	1704 pyrazo. 1679 quinaz. 1666 amide	1646	ν(C-Br) 655
16		288-289	92	Light orange	3377	1703 pyrazo. 1677 quinaz. 1662 amide	1641	$\nu(NO_2)$ asy.1523 sym.1365

Synthesis of 2-phenyl-3-[2-acetamido-4-phenyl-2-hydrazinyl-(4,6-dimethyl-2-oxopyrimidin-5(2H)-ylidene)]-quinazolin-4(3H)-one[17] and 2-phenyl-3-[2-acetamido-4-phenyl-2-hydrazin yl-(4,6-dimethyl-2-thioxopyrimidin-5(2H)-ylidene)]-quinazolin-4(3H)-one[18][(24)].

Urea or thiourea (0.0006mol) was added with continuous stirring to the solution of compound [5](0.3g, 0.0006mol) dissolved in (3mL) pyridine. The mixture was refluxed for (6-8) hours and poured into cold diluted

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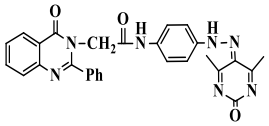
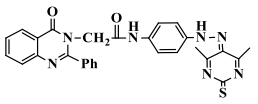
HCl. Then the solid product separated by filtration. The precipitate washed with distilled water and recrystallized from acetone. Physical properties and FTIR spectral data were listed in table (5).

Table 5: Physical properties and FTIR spectral data cm^{-1} of compounds (17-18)

Com. No.	structure	Physical properties			FTIR absorption cm^{-1}			
		M.P. ^{o}C	Yield %	Color	ν(N-H)	ν(C=O)	ν(C=N)	Others
17		175-177	74	White	3237	1706 pyrim. 1691 quinaz. 1685 amide	1624	ν(C=C) aromatic 1591 1531
18		180-181	86	Off white	3238	1696 quinaz. 1670 amide	1628	ν(C=S) Pyrim. 1487

Antimicrobial activity

Some of synthesized compounds were screened for their antibacterial and antifungal activities against the various bacteria (gram-negative species (*Escherichia coli* , *Pseudomonas aeruginosa*, and gram-positive species *Staphylococcus aureus* , *Bacillus subtilis*) and fungal strain *(candida tropicalis*) . The antimicrobial activity carried out by Agar well diffusion method using (28g /1000 mL D.W) Mueller-Hinton agar (MHA) medium and (65g /1000 mL D.W) Sabouraud's Dextrose agar (SDA) medium for bacteria and fungi strain respectively, that impregnated with microbial suspention by swab. Then a wells with diameter equal to 8mm is punched with a sterile cork borer. (100µL) of tested compounds solution (800µg/ml) introduced into holes. The inoculated plates were incubated at 37 ^{o}C for 24 hours. Negative control were prepared using the same solvent DMSO that dissolved the tested compounds. Ciprofloxacin and Clotrimazole (800µg/mL) were used as positive standard to determined the sensitivity of each microbial test. Antimicrobial activity estimated by measuring the diameter of zone of inhibition against test organisms as shown in table (9).

II. RESULTS AND DISCUSSION

New pyrazole, pyrazolinone and pyrimidine derivatives linked to quinazolinone ring were designed started by prepared the quinazolin-4(3H)-one skeleton in three steps. The first step involved nucleophilic addition and elimination reaction between anthranilic acid and benzoyl chloride in dry and cold conditions to prepared compound [1] that treated in second step with acetic anhydride to gave compound [2], then under nucleophilic substitution reaction of compound [2] with ethyl glycinate in presence of dry pyridine, compound [3] was prepared in third step as in scheme (1).

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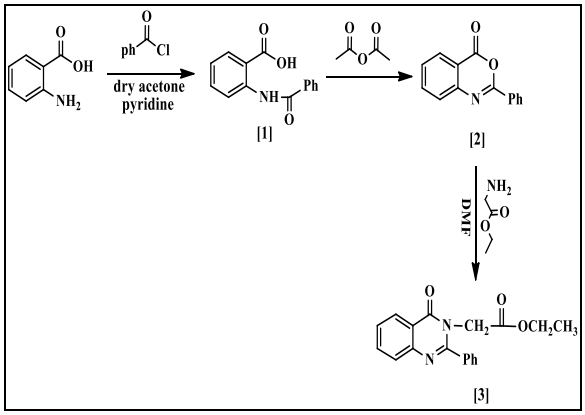
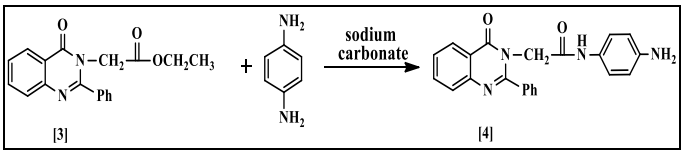


Scheme 1: Synthesis of quinazolin-4(3H)-one nucleus

The characteristic evidence to formation compound [3] is positive test with hydroxamic acid [25]. FTIR spectrum for compound [3] shown ν(C-H) aliphatic at (2989, 2902) $cm^{-1}$and two strong stretching vibration band at (1739) cm^{-1} and (1683) cm^{-1} due to (C=O ester) and (C=O amide) respectively. (1643) cm^{-1} belonged to ν(C=N). The characteristic data of FTIR spectrum were listed in table (1). ^{1}H-NMR spectrum of this compound showed triplet signal at δ= 1.29 ppm due to methyl protons, quartet signal at δ=2.50 ppm for (O-C<u>H</u>$_2$), doublet signal due to (N-C<u>H</u>$_2$-C=O) protons at δ= 4.35 ppm and multiplet signal refer to nine aromatic protons at δ= (7.23-7.98) ppm .^{13}C-NMR spectral data were recorded in table (6).

Compound [4] was formed by treated of Compound [3] with p-phenylenediamine in presence of sodium carbonate as shown in equation (1).



Equation 1: Synthesis of p-phenylenediamine derivatives

FTIR spectrum of compound [4] showed special band appearance at (3469, 3421) cm^{-1} belonged to the asymmetric and symmetric stretching vibration of (NH_2) group, 3315 cm^{-1} due to ν(N-H) [26], (1687) cm^{-1} belonged to carbonyl group of amide, at (1643) cm^{-1} for t ν(C=N). The FTIR absorption data were listed in table (2). ^{1}H-NMR spectrum of this compound showed at δ= 4.30 ppm and δ= 4.59 ppm two singlet signal belonged to (N-C<u>H</u>$_2$-C=O) and (N<u>H</u>$_2$) protons respectively, multiplet signal belonged to the protons of aromatic rings at δ= 7.19-8.06 ppm, (N<u>H</u>) proton indicated at δ= 8.53 ppm.^{13}C-NMR data information were recorded in table (6).

Compounds [5] and [6] was prepared from coupling reaction between diazonium salt and active methylene acetyl acetone, ethyl acetoacetate compounds respectively as shown in scheme (2).

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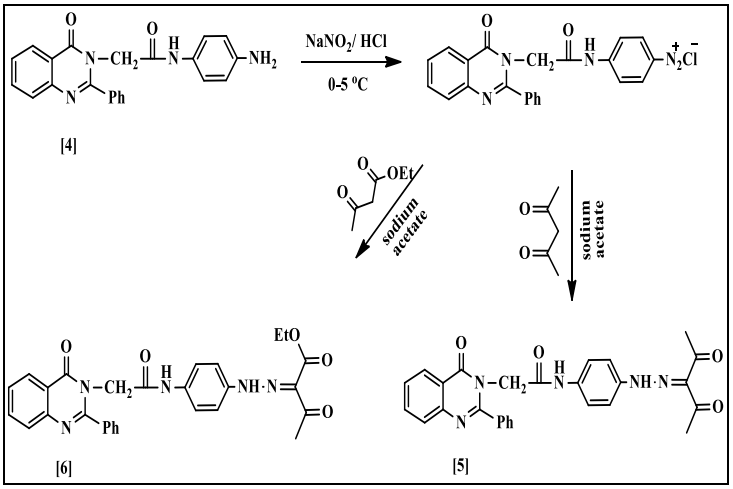
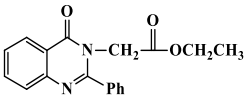
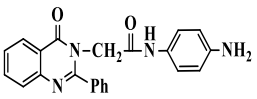
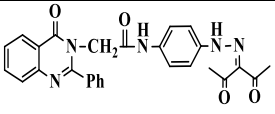


Scheme 2: Synthesis of compounds [5] and [6]

FTIR spectrum of compound [5] showed absorption bands at (3431, 3400) cm^{-1} belonged to ν(N-H) and two appearance bands at (1724) cm^{-1} and (1676) cm^{-1}due to (C=O ketone) and (C=O amide) respectively, (1648) cm^{-1} for ν(C=N), also at (1600, 1533) cm^{-1} due to aromatic (C=C). Compound [6] showed absorption band at (3429) cm^{-1} belonged to ν(N-H) and three appearance bands at (1735) cm^{-1}, (1716) cm^{-1} and (1672) cm^{-1} due to (C=O ester), (C=O ketone) and (C=O amide) respectively, (1633) cm^{-1} for ν(C=N), (1608,1591) cm^{-1} due to aromatic (C=C). All FTIR spectral data of compounds [5] and [6] were listed in table (2). ^{1}H-NMR spectral of compound [5] showed singlet signal due to (2C<u>H</u>$_3$) protons at δ equal to 3.40 ppm, a (N-C<u>H</u>$_2$-C=O) protons appeared at δ=4.33 ppm, at chemical shift 7.10 ppm a singlet signal indicated for (N<u>H</u>-N hydrazinyl) proton, δ=(7.20-8.53) ppm due to (Ar-<u>H</u>) and singlet signal at δ=8.78 ppm for (O=C-N<u>H</u> amide). ^{13}C-NMR spectral data of compounds [5] were recorded in table (6).

Table 6: ^{1}H-NMR and ^{13}C-NMR spectral data (δ ppm) of compounds (3,4,5)

Com. No.	**structure**	**^{1}H-NMR spectral data (δ ppm)**	**^{13}C-NMR spectral data (δppm)**
3		1.29(t,3H,CH_3); 2.50(q,2H,O-CH_2); 4.35(s,2H,N-CH_2-C=O); 7.23-7.98(m,9H,Ar-H)	14.40(CH_3); 41.86(O-CH_2); 61.86(N-CH_2-C=O); 117.54-134.90(Ar-C); 140.77(C=N quinaz.) 165.18 O=C-N quinaz.) 169.70(O=C-O ester)
4		4.30(s,2H,NH_2); 4.59(s,2H,N-CH_2-C=O); 7.19-8.06(m,13H,Ar-H); 8.53 (s,1H,NH)	61.95(N-CH_2-C=O); 116.50-134.90(Ar-C); 152.59(C=N quinaz.); 165.32(O=C-N quinaz.); 171.16(O=C-NH amide)
5		3.40(s,6H,2CH_3); 4.33(s,2H,N-CH_2-C=O); 7.10(s,IH,NH-N hydraz.); 7.20-8.53(m,13H,Ar-	50.38(2CH_3); 68.19(N-CH_2-C=O); 111.56-135.71(Ar-C); 153.94(C=N quinaz.);

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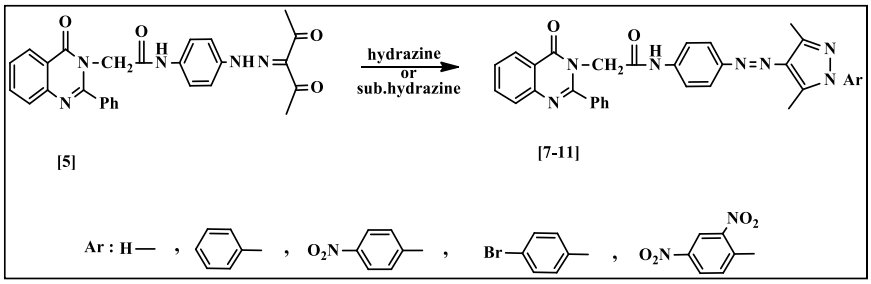
		H); 8.78(s,1H,O=C-NH amide)	161.62(O=C-N quinaz.); 168.59(O=C-NH amide); 182.57(2(O=C) ketone)

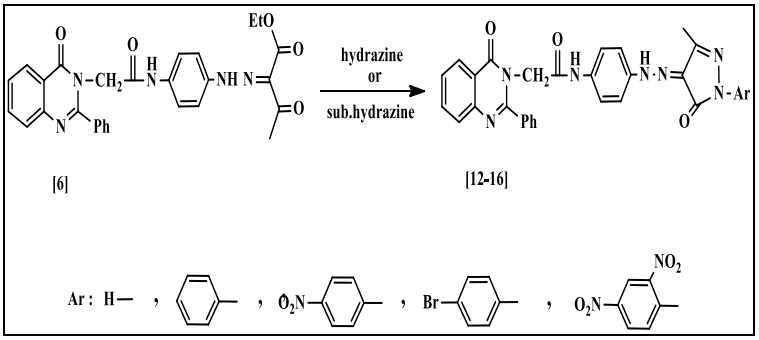
Pyrazole derivatives [7-11] afforded from cyclization reaction of hydrazono acetyl acetone [5] with hydrazine and substituted hydrazine as shown in equation (2).



Equation 2: Synthesis of pyrazole derivatives

FTIR spectrum of compounds [7-11] showed the appearance of the absorption bands at (3325-3247) cm^{-1} belonged to ν(N-H), (1696-1689) cm^{-1} due to ν(C=O quinazolinone ring), (1680-1669) cm^{-1} due to ν(C=O amide), (1654-1624) cm^{-1} belonged to ν(C=N), (1450-1444) cm^{-1} for ν(N=N). More FTIR spectral data of compounds [7-11] listed in table (3). ^{1}H-NMR spectral of compound [7] showed a singlet signal at chemical shift equal to 3.37 ppm for (2C<u>H</u>$_3$- pyrazole ring) protons, at δ= 4.67 ppm a singlet signal for (N-C<u>H</u>$_2$-C=O) protons, δ=(7.14-8.06) ppm due to (Ar-<u>H</u>) protons, a singlet signal at δ=8.63 ppm belonged to (O=C-N<u>H</u> amide) proton, at δ=10.17 ppm due to (N<u>H</u> pyrazole) proton. ^{1}H-NMR, ^{13}C-NMR spectral data were recorded in table (7).

The formation of pyrazolinone derivatives [12-16] including cyclized of hydrazono ethylaceto acetate compound [6] with hydrazine and substituted hydrazine as shown in equation (3).



Equation 3: Synthesis of pyrazolinone derivatives

FTIR spectrum of compounds [12-16] showed the appearance of the absorption bands at (3377-3238) cm^{-1} belonged to ν(N-H), (1704-1700) cm^{-1} due to (C=O pyrazole ring), (1690-1677) cm^{-1} due to ν(C=O quinazolinone ring), (1670-1662) cm^{-1} due to ν(C=O amide), (1648-1635) cm^{-1} belonged to ν(C=N) . More FTIR spectral data of compounds [12-16] listed in table (4). ^{1}H-NMR spectrum of compound [15] showed a singlet signal at chemical shift equal to 3.28 ppm for (C<u>H</u>$_3$- pyrazolinone ring) protons, at δ= 4.31 ppm a singlet

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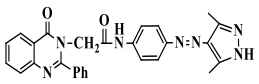
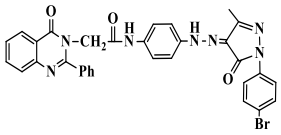
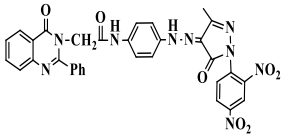
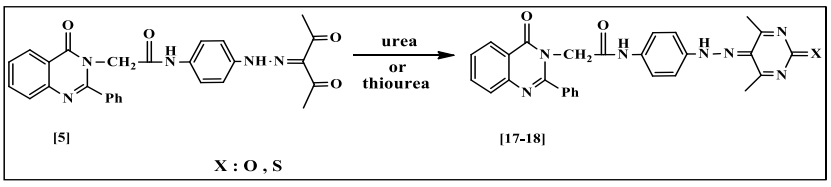
signal for (N-C<u>H</u>$_2$-C=O) protons, a singlet signal at δ= (7.19) ppm belonged to (N-N<u>H</u> hydrazinyl) δ=(7.20-8.06) ppm due to (Ar-<u>H</u>) protons, a singlet signal at δ=8.52 ppm belonged to (O=C-N<u>H</u> amide) proton. Compound [16] showed singlet signal due to (C<u>H</u>$_3$) protons at δ equal to 3.30 ppm, a (N-C<u>H</u>$_2$-C=O) protons appeared at δ=4.33 ppm, at chemical shift 7.20 ppm a singlet signal indicated for (N<u>H</u>-N hydrazinyl) proton, δ=(7.22-8.23) ppm due to (Ar-<u>H</u>) and singlet signal at δ=8.81 ppm for (O=C-N<u>H</u> amide). ^{1}H-NMR, ^{13}C-NMR spectral data were recorded in table (7).

Table 7: ^{1}H-NMR and ^{13}C-NMR spectral data (δ ppm) of compounds (7,15,16)

Com. No.	structure	^{1}H-NMR spectral data (δ ppm)	^{13}C-NMR spectral data (δppm)
7		3.37(s,6H,2CH$_3$); 4.67(s,2H, N-CH$_2$-C=O); 7.14-8.06(m,13H,Ar-H); 8.63(s,1H,O=C-NH amide); 10.17(s,1H,NH pyraz.)	54.17(2CH$_3$); 65.52(N-CH$_2$-C=O); 119.63-139.77(Ar-C); 154.23(C=N quinaz.); 164.85(O=C-NH quinaz.); 169.70(O=C-NH amide)
15		3.28(s,3H,CH$_3$); 4.31(s,2H,N-CH$_2$-C=O); 7.19(s,1H,N-NH hydraz.); 7.20-8.06(m,13H,Ar-H); 8.52(s,1H,O=C-NH amide)	53.32(CH$_3$); 61.96(N-CH$_2$-C=O); 121.37-136.16(Ar-C); 156.38(C=N quinaz.); 160.55(O=C-N pyraz.); 163.80(O=C-N quinaz.); 167.06(O=C-NH amide)
16		3.30(s,3H,CH$_3$); 4.33(s,2H,N-CH$_2$-C=O); 7.20(s,1H,NH-N hydraz.); 7.22-8.23(m,13H,Ar-H); 8.81(s,1H, O=C-NH amide)	56.56(CH$_3$); 64.91(N-CH$_2$-C=O); 117.90-136.62(Ar-C); 149.72(C=N quinaz.); 162.71(O=C-N pyraz.); 165.04(O=C-N quinaz.); 171.60(O=C-NH amide)

pyrimidine derivatives [17-18] prepared from cyclization of hydrazono acetyl acetone [5] with urea and thiourea in pyridine solvent as shown in equation (4).



Equation 4: Synthesis of pyrimidine derivatives

FTIR spectrum of compound [17] showed the appearance of the stretching vibration band at (3237) cm^{-1} due to ν(N-H), (1706, 1691 and 1685) cm^{-1} belonged to ν(C=O) for pyrimidine ring, quinazolinone ring and amide, (1624) cm^{-1} due to (C=N), (1591, 1531 and 1494) cm^{-1} for aromatic (C=C). Compound [18] showed the appearance of the stretching vibration band at (3238) cm^{-1} due to ν(N-H), (1696, 1670) cm^{-1} belonged to ν(C=O)

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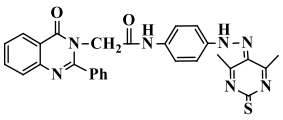
for quinazolinone ring and amide, (1628) cm^{-1} due to (C=N), (1487) cm^{-1} indicated the thiocarbonyl group of pyrimidine ring. All FTIR spectral of compounds [17, 18] are listed in table (5). ^{1}H-NMR spectral of compound [18] showed singlet signal at δ= 3.29 ppm due to ($C\underline{H}_3$) protons, δ= 4.32 ppm for (N-$C\underline{H}_2$-C=O) protons, δ=7.14 ppm due to (N$\underline{H}$-N hydrazinyl) proton, multiplet signal at δ= (7.18-7.97) ppm for (Ar-$\underline{H}$) protons, a singlet signal at 8.45 ppm for (O=C-N$\underline{H}$) amide. ^{13}C-NMR spectral data were recorded as shown in table (8).

Table 8: ^{1}H-NMR and ^{13}C-NMR spectral data (δ ppm) of compound (18)

Com. No.	**structure**	**^{1}H-NMR spectral data (δ ppm)**	**^{13}C-NMR spectral data (δppm)**
18		3.29(s,6H,2CH_3); 4.32(s,2H,N-CH_2-C=O); 7.14(s,1H,NH-N hydraz.); 7.18-7.97(m, 13H,Ar-H); 8.45(s,1H,O=C-NH amide)	49.85(2CH_3); 64.79(N-CH_2-C=O); 115.16-134.82(Ar-C); 157.26(C=N quinaz.); 164.23(O=C-Nquinaz.); 167.45(O=C-NH amide); 190.27(C=S pyrim.)

Anti microbial activity

Based on the results in table (9), synthesized new derivatives show significant inhibition action on the growth of different bacteria when compared with reference standard. While some of them showed no activity. These compounds exhibited good antifungal activity against *Candida tropicalis* fungi.

Table 9: Antimicrobial activity of some synthesized compound

Compounds (800µg/mL) and standard (800µg/mL)	**Zone of inhibition (mm)**				
	Pseudomonas aeruginosa	**Escherichia coli**	**Bacillus subtilis**	**Staphylococcus aureus**	**Candida tropicalis**
5	18	14	34	-	30
6	30	22	20	24	18
7	19	6	-	18	10
9	31	29	8	20	26
10	10	28	22	30	22
12	20	16	16	16	19
13	-	12	32	32	20
17	18	32	13	8	24
DMSO	-	-	-	-	-
Ciprofloxacin	29	27	30	31	-
Clotrimazole	-	-	-	-	20

Zone of inhibition: (-) no inhibition , (3-6) weak inhibition , (7-10) moderate , (11-15) strong

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III. CONCLUSION

The present work led to:

- Synthesis a new series of N-substituted pyrazole, pyrazolinone and pyrimidine derivatives containing quinazolinone through multi steps chemicals reactions.
- Structure of prepared compounds were characterized by FTIR and NMR spectra.
- The prepared derivatives were screened for antibacterial and antifungal activities by agar well diffusion method against *Escherichia coli* , *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Bacillus subtilis* also a fungal strain *candida tropicalis*.
- In vitro biological activity data showed good results spesically as antifungal agents.

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