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Design – Syntheses, Characterization and Evaluation Antimicrobial Activity for Some azobenzen-p, p'-disubstituted with (3, O), (3, N-) substitute, (3, H) -quinazolin-4-one-2yl and 4-substituted quinazolin-2yl moieties

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Abstract: ***Two of 3, O-substituted quinazoline-4-one namely azobenzen-p, p'-di[3, O-benzyl-4 (3H) quinazolin-4-one-2yl], and azobenzen-p, p'-di[3, O-acetyl-4 (3H) quinazolin-4-one-2yl], were synthesized from azobenzen-p, p'-di[3-hydroxy-4 (3H) quinazolin-4-one-2yl]. Two of 3-N-substituted quinazoline-4-one namely azobenzen-p, p'-di[3, N-benzensulphonylamide-4 (3H) quinazolin-4-one-2yl], and azobenzen-p, p'-di[3, N- (4'-nitrofurfurylidine-2'-yl imino) -4 (3H) quinazolin-4-one-2yl], were synthesis from azobenzen-p, p'-di[3-amino-4 (3H) quinazolin-4-one-2yl]. azobenzen-p, p'-di[3-hydro-4 (3H) quinazolin-4-one-2yl], was synthesized from azobenzen-p, p'-di (3, 1-benzoaxzine-4-one-2yl], which was used for synthesis azobenzen-p, p'-di[4-chloro-quinazolin-2yl], while its treatment with p-toluidine and ethylene diamine give azobenzen-p, p'-di[4-N-toludino-quinazolin-2yl], and azobenzen-p, p'-di[4-N-aminoethylamine-quinazolin-2yl] respectively. All synthesized compounds characterized by FTIR, ^{1}HNMR, ^{13}CNMR and mass spectral analyses. All synthesized compounds, were examined as antibacterial agents against gm (+ve and –ve) bacteria, and antifungal agents. Results showed abroad extended excellent to moderate effects as antibacterial and antifungal agents.***

Keywords: di-substituted-quinazolinone, antibacterial, antifungal

1. Introduction

One of the most important features in 3, 1-benzoxazin-4-ones chemistry is their uses as starting materials key for further transformations; they are indeed useful intermediates in organic synthesis [1-7]. Its reaction with nitrogen nucleophiles gives 4 (3H) quinazolinones [8-9]. The quinazolinone moiety is an important pharmacophore showing many types of pharmacological activities, the quinazolines are considered to be "privileged structure" for drug development [10-12]. They also exhibit a wide range of activities [13-15]; such as anticonvulsant, anti-inflammatory, anti-malarial, anti-sedative, Analgesic, anti-oxidant, anti-cancer, anti-microbial, anti-bacterial, anti-fungal, anti-mycobacterial, anthelmintic, muscle relaxant, anti-hyperlipidemic, anti-tubercular, anti-tumor, hypotensive activities [16-29]. also quinazoline and its derivatives are very important and vital group of chemotherapeutical drugs such as anti-histamine, anti-allergy and anti-diabetic, as well as quinazolinone and its derivatives exhibited a good activity as anti-fibrillatory [30-32]. Quinazolinone moiety is present in many commercialized drugs such as Albaconazole, Gifitinib [33-36]. Besides several quinazoline derived clinical candidates are in various stages of development [37].

2. Material and Methods

1- Syntheses of azobenzen-p, p´-di[3-substituted-4 (3H) -quinazolinone-2yl] [38]:

A mixture of azobenzen-p, p´-di[3, 1-benzoxazine-4-one-2yl] (0.472gm: 0.001 mol), and amino moieties compounds, like, hydroxylamine hydrochloride, hydrazine hydrate (0.002 mol), DMF (25ml), were refluxed for a time [mentioned in table (1)], until completion of reactions were monitored by TLC using petroleum ether: ethyl acetate [3:2] eluent. Solids were separated, filtered and purified by crystallization from DMF, to give azobenzen-p, p´-di[3-substituted -4 (3H) -quinazolinone-2yl][1, 2].

Table 1: details of azobenzene-p, p´-di[(3-substituted) - 4 (3H) quinazolinone-2yl] compounds [1, 2]

No.	Name of compounds	Weight of product	Yield %	color	m.p ℃
1	Azobenzen-p, p'-di[3-hydroxy-4 (3H) [qunazolinone-2yl	0.4 gm	78	Pale orange	272
2	Azobenzen-p, p'-di[3-amino-4 (3H) [qunazolinone-2yl	0.53 لة	88	yellow	340

2- Synthesis of azobenzen-p, p´-di[3, O-subsitituted-4 (3H) quinazolinone-2yl][1a, 1b]:

To a solution of azobenzen-p, p´-[3-hydroxy-4 (3H) -quinazolinone-2yl][1] (0.5 gm, 0.001 mol), in DMF (20ml), freshly distilled Acetyl chloride 1.56ml, or benzyl chloride 0.25ml equivalent 0.002mol), and sodium hydroxide (0.1gm), were added. Reaction mixture was refluxed for 3hrs, until completion of reaction which was monitored by TLC using petroleum ether:ethyl acetate [3:2] eluent. Precipitate was formed, filtered and washed with distilled water, recrystallized from DMF, to give compounds [1a], 0.41gm, yield; 60%, m.p. 218-220℃, and compound [1b], 0.38gm, yield; 55.71%, m.p. 249-251℃ respectively.

3- Synthesis of azobenzen-p, p'-di[3, N-substituted-4 (3H) quinazolinone-2yl][2a, 2b]:

A- To a solution of azobenzen-p, p'-di[3-amino-4 (3H) quinazolinone-2yl][2] (0.5gm, 0.001mol), in DMF (10ml), containing dry pyridine (3ml), benzenesulfonyl chloride, (0.2ml, 0.002mol), was added in small portions, reaction mixture was reflexed for 6hrs, until completion of reaction which was monitored by TLC using petroleum ether: ethyl acetate [3:2] eluent. Reaction mixture was cooled, poured slowly into stirred ice-cold water, and kept in refrigerator for 1/2h. The precipitate was formed, filtered, washed with distilled water and dried. Then recrystallized from DMF, to give compound [2a]. 0.32gm, yield; 42%, m.p. 301-303℃.

B- To a stirred solution of azobenzen-p, p'-di[3-amino-4 (3H) quinazolinone-2yl] (0.5gm, 0.001mol), in DMF (20ml), glacial acetic acid (3drops). A solution of 5-nitro-2-furaldehyde (0.274gm, 0.002mol) in ethanol (10ml), was added slowly. Reaction mixture was stirred for 8hrs, until completion of reaction which was monitored by TLC using petroleum ether: ethyl acetate [3:2]eluent. Precipitate was formed, filtered and washed with distilled water, recrystallized from DMSO, to give compound [2b]. 0.38gm, yield; 52%, m.p. 211-213℃.

4- Synthesis of azobenzen-p, p'-di[3-hyrdo-4-quinazolinone-2yl] [3]:

A mixture azobenzen-p, p'-di[3, 1-benzoxazine-4-one-2yl][38] (0.472gm, 0.001mol) in DMF (20ml), ammonium acetate (0.154gm, 0.002mol), ammonium hydroxide (38%), (4mL) and 10% sodium hydroxide (5mL), pyridine (15mL), was heated under reflux for 8hrs, until completion of reaction which was monitored by TLC using petroleum ether: ethyl acetate [3:2] eluent, and then left to cold. Reaction mixture was then triturated with cold distilled water (100mL) and neutralized with 1N HCl (5mL), resulting precipitate was collected by filtration, washed with water, dried and recrystallized from DMF, to give compound [3]. 0.36gm, yield; 76%, m.p. 190-192℃

5- Synthesis of azobenzen-p, p´-di[4-chloro-quinazolin-2yl] [4]:

A mixture of azobenzen-p, p'-di[3-hyrdo-4H-quinazolinone-2yl [3] (0.47gm, 0.001mol), phosphorouspentachloride (0.416gm, 0.002mol), phosphorousoxychloride (20mL), containing dry pyridine (5ml), was heated on a water bath for 6hrs, until completion of reaction which was monitored by TLC using petroleum ether: ethyl acetate [3:2] eluent. Reaction mixture was poured gradually on crashed ice. The separated solid was filtered off, dried then recrystallized from DMF to give compound [4]. 0.35gm, yield; 69%, m.p. 236℃.

6- Synthesis of azobenzen-p, p´-di[4-substituted-quinazolin-2yl] [4a, 4b]:

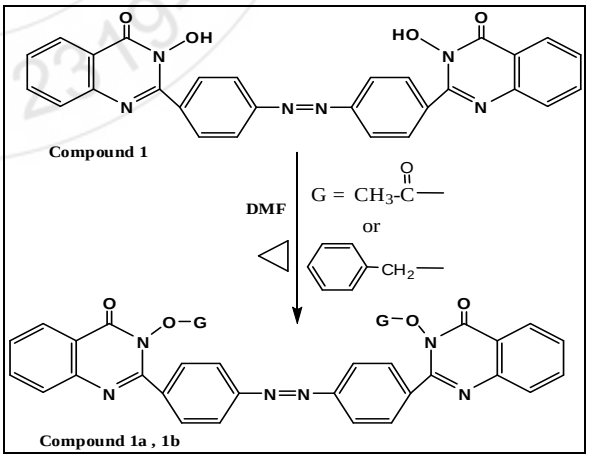
A mixture of azobenzen-p, p´-di[4-chloro-quinazoline-2yl][4] (0.507gm, 0.001mol) and amino-moieties like [p-toluidine (2.1gm) or 1, 2-diaminoethanedihydrochloride (0.27gm) equivalent to (0.002mol)] respectively in DMF (20mL) were reflexed for 6hrs, until completion of reaction which was monitored by TLC using petroleum ether: ethyl acetate [3:2] eluent. Separated solid was filtered off, dried then recrystallized from DMF to give compound [4a], 0.4gm, yield 61.7%, m.p.285℃ and compound [4b] 0.38gm, yield 69.4%, m.p.307℃ respectively.

3. Result and Discussion

Chemistry of quinazoline, quinazolin-4-one and their derivatives have much considerable importance, due to effectiveness in biological and pharmacological fields. Because off these reason, we design to synthesis some of new (3, O-), (3, N-) substituted quinazolin-4-one-2yl and 4-substituted quinazoline-2yl moieties, substituted at (p.p') -positions of bridged azobenzene molecule.

A. First: azobenzen-p, p'-di[3-hydroxy-4- (3H) quinazolin-4-one-2yl], was synthesized and characterized as in published paper [38]

Second: Synthesis of azobenzen-p, p´-di[3, O-subsitituted-4 (3H) quinazolinone-2yl][1a, 1b]:



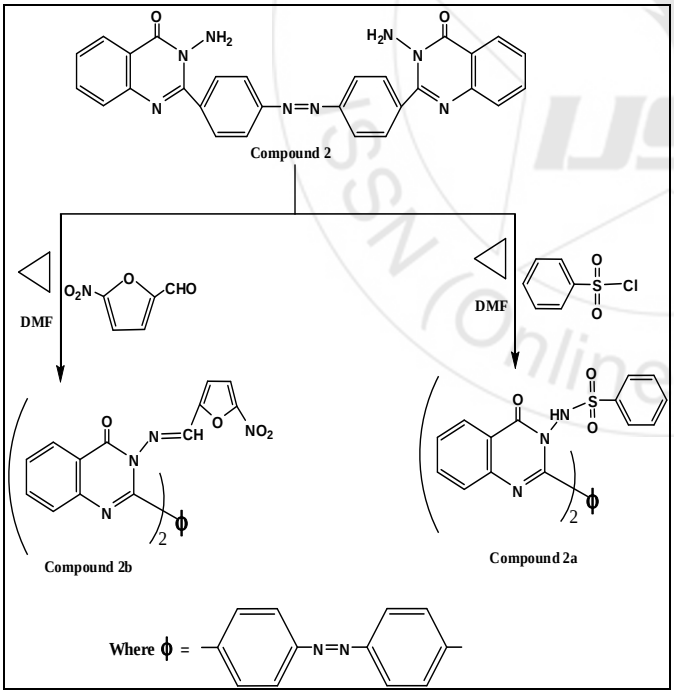
Condensation of azobenzen-p, p'-di[3-hydroxy-4 (3H) quinazolinone-2yl] [1] with benzyl chloride or acetyl chloride in a molar ratio (1:2), give azobenzen-p, p'-di[3, O-benzyl-4 (3H) quinazolinone-2yl] [1a] and azobenzen-p, p'-di[3, O-acetyl-4 (3H) quinazolinone-2yl] [1b] respectively. These compounds are characterized by FTIR, ^{1}H NMR, and ^{13}C NMR spectral analysis. FTIR- spectral analysis of compounds

[1a], showed stretching band of azo (N=N) group at 1446 cm^{-1}, beside quinazolinone ring stretching C=O and C=N bands at 1670, 1620 cm^{-1} respectively. But ^{1}H NMR- spectrum of compounds [1a], showed quinazolinone ring and phenyl ring protons as multiple (26H) protons, at δ (6.9 - 8.7) ppm, beside two methylene protons as (4H) protons at δ (3.5) ppm. While ^{13}C NMR- spectrum of this compound showed quinazolinone carbon as aromatic, (C=O), (C=N) carbons signal at δ (109 - 145), (168), (153) ppm respectively, beside methylene ($-CH_2$) carbon at δ (71) ppm [39].

FTIR- spectral analysis of compound [1b], showed carbonyl of (CH_3-CO) bands and azo (-N=N-) stretching bands at (1712, 1473) cm^{-1}, as well as to quinazolinone (C=O), (C=N) stretching bands at (1674 and 1604) cm^{-1} respectively. ^{1}H NMR- spectrum of compound [1b], showed quinazolinone ring protons as a multiple (16H) at δ (6.7 – 8.2) ppm, and methyl protons of acetyl groups as a singlet signal at δ (3.2) ppm. ^{13}C NMR- spectrum of this compound showed quinazolinone ring as aromatic carbonyl carbon of (C=O), and (C=N) carbons as a multiple signals at δ (111 - 145) ppm, and singlet signals at δ (165 and 153) ppm respectively, beside carbon signal of methyl group at δ (70) ppm.

B. First: azobenzen-p, p'-di[3-amino-4- (3H) quinazolin-4-one-2yl], was synthesized and characterized as in published paper [38].

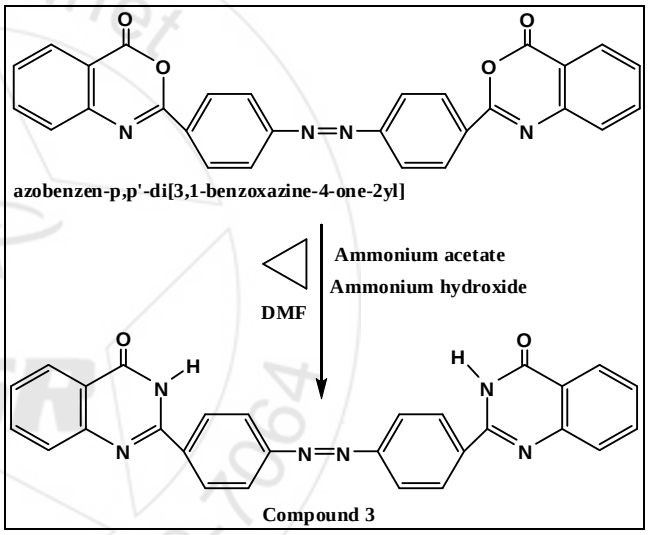
Second: Synthesis of azobenzen-p, p'-di[3, N-substituted-4 (3H) quinazolinone-2yl][2a, 2b]:



Azobenzen-p, p'-di[3, N-benzenesulphonamido-4 (3H) quinazolinone-2yl] [2a], was synthesized by condensation of azobenzen-p, p'-di[3-amino-4 (3H) quinazolinone-2yl] [2] with benzenesulphonyl chloride in a molar ratio (1:2), characterized by FTIR, ^{1}H NMR, and ^{13}C NMR spectral analysis. FTIR- spectral analysis of this compound [2a] showed stretching frequency of quinazolin ring C=O and C=N bands at 1674 and 1620 cm^{-1} respectively, beside sulphonamido (NH) and azo (N=N) stretching bands at 3271 and 1446 cm^{-1} respectively. ^{1}H NMR- spectrum of this compound, showed all aromatic (-CH) and (-NH) sulphonamido proton as a cluster of multiple (28 H) signals at a range δ (6.8 - 9.1) ppm. While ^{13}C NMR- spectrum of compound [2a] showed aromatic (-CH), carbonyl carbon (C=O), and azomethine (C=N) carbon signals of quinazolin ring as multiple at δ (117 - 132), singlet signal at δ (172) and (153) ppm respectively.

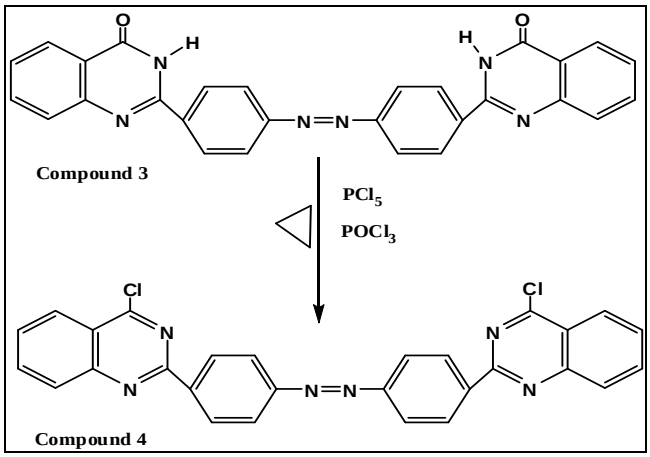
While Azobenzen-p, p'-di[3, N (4′-nitrofurfuryldin-2′-yl-imino) -4 (3H) -quinazolinone-2yl] [2b], FTIR- spectrum, showed stretching frequency of quinazolin ring C=O and C=N bands at 1635 and 1581 cm^{-1} respectively, as well as starching bands of azo N=N group at 1442 cm^{-1}, and asymmetric and symmetrical starching bands of NO_2 at 1508, 1338 cm^{-1} respectively.

C- Synthesis of azobenzen-p, p'-di[3-hydro- (4H) -quinazolinone-2yl] [3]:



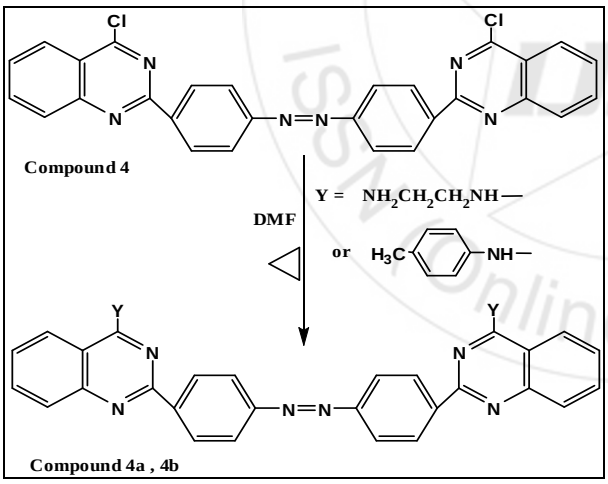
Condensation of azobenzen-p, p'-di[3, 1-benzoxazin-4-one-2yl] with excess of ammonia and ammonium acetate in DMF, in a molar ratio (1:2), gave azobenzen-p, p'-di[3-hydro- (4H) -quinazolinone-2yl] [3], which was characterized by FTIR, ^{1}HNMR, ^{13}CNMR, and mass spectral analysis. FTIR- spectral analysis of compound [3], showed azo-group (N=N) at (1452) cm^{-1}, beside 3-hydro-4-quinazolinone ring starching bands (NH), (C=O), and (C=N), at (3267, 1661, 1600 cm-1) respectively. ^{1}H NMR- spectrum of this compound, showed aromatic (CH), and (NH) quinazolinone protons as a multiplet signals of (18H) at (6.9 - 8.8) ppm. While ^{13}C NMR-spectrum of compound [3], showed aromatic carbon of quinazolinone (C=O), and azomethine (C=N) carbons as a multiplet signals at δ (115 - 143), singlet signal at (172), and (153) ppm, respectively. Mass spectral analysis of compound [3], showed $M^{\cdot+2}$ ion at m/z (470) in the extensional part of this spectrum (using NL:8.01E6).

D- Synthesis of azobenzen-p, p'-di[4-chloro-quinazolin-2yl] [4]:



Treatment of azobenzen-p, p'-di[3-hydro-4-quinazolinone-2yl] [3] with phosphorus pantachloride / phosphorus oxychloride, give azobenzen-p, p'-di[4-chloro-quinzoline-2yl] [4], which characterized by FTIR, and mass spectral analysis. FTIR- spectrum of this compound [4], showed azo starching band (N=N) at 1435 cm^{-1}, beside quinazolin (C=O) and (C=N) starching bands at 1674 and 1593 cm-1 respectively. Mass spectrum of compound [4], showed molecular ion M^{+2} at m/z (507), in the extensional part of this spectrum using (NL:1.6E5).

E- Synthesis of azobenzen-p, p'-di[4-substituted-quinazolin-2yl][4a, 4b]:



Substitution reaction of chlorine in azobenzen-p, p'-di[4-chloro-quinazolin-2yl] [4], with p-toluidine or ethylenediamine, give azobenzen-p, p'-di[4, N-toluidino-quinazolin-2yl] [4a] and azobenzen-p, p'-di[4, N-aminoethylamine-quinazolin-2yl] [4b] respectively. Azobenzen-p, p'-di[4, N-toluidino-quinazolin-2yl] [4a], was characterized by FTIR, ^{1}H NMR and ^{13}C NMR spectral analysis.

FTIR- spectral analysis of compound [4a], showed (NH) stretching bands of amino group (NH) and azo (N=N) at (3200, 1454) cm^{-1} respectively, beside quinazolin (C=N) stretching bands at (1631, 1543) cm^{-1} respectively. While ^{1}H NMR- spectrum of this compound [4a], showed singlet signal of methyl protons at δ (4.01) ppm, as well as aromatic ring (CH) proton and amino proton as a multiplet signal of (26H) proton at δ (6.8 - 8.9) ppm. But ^{13}C NMR- spectrum of this compound showed methyl carbon (CH_3) as a singlet signal at δ (93) ppm, beside quinazolin ring (aromatic carbon and azomethine carbon (C=N) carbon) as a multiplet signals at δ (117 - 145 and 153) ppm respectively.

FTIR-spectrum of compound [4b], showed both (NH) and (NH_2) starching bands at 3481-3431, 3282 cm^{-1} and azo starching band (N=N) at 1431 cm^{-1}, beside quinazolin ring azomethine (C=N) at 1621, 1598 cm^{-1} respectively.

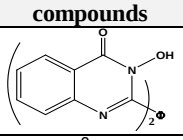
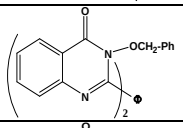
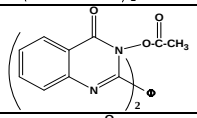
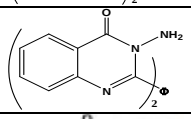
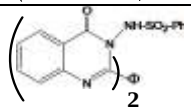
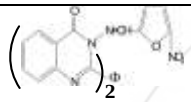
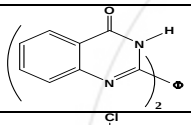
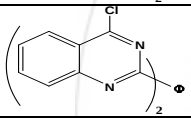
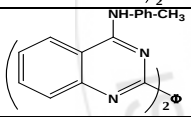
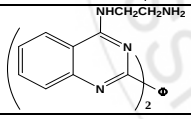
F- Anti-microbial studies:

Synthetic compounds [1, (1 (a, b), 2, 2 (a, b), 3, 4, 4 (a, b)], were examined as antibacterial agents against gm (+ ve) Staphylococcus aurous, Bacillus bacteria, and gm (- ve) Escherichia coli, Klesbsiella pneumonia bacteria, in comparison with effect of Cephalexin, Amoxicillin, Tetracycline Lincomycin antibiotics. Also these were examined as antifungal agents against Aspergillus flavs and Penecillium fungi in comparison with the effect of Nystatin and Fluconazole antifungal treatments.

According to the results given in Table (2), following observation would be deduced:

First: All synthesized compounds, except (1b), were found to have excellent effect on gm (+ve) Bacillus bacteria in comparison with antibiotics.
Second: All synthesized compounds, were found to have very good to good effect on gm (+ve) Staphylococcus aurous bacteria, specially compounds (1, 1b, 2, 2a & 3), in comparison with antibiotics.
Third: All synthesized compounds, except (1, 2, 4), were found to have good to very good effect on gm (-ve) Escherichia coli bacteria, specially (1b and 2b) in comparison with antibiotics.
Fourth: All synthesized compounds, except (1b, 2b, 4), were found to have moderate effect on gm (-ve) Klebsiella pneumonia bacteria in comparison with antibiotics.
Fifth: All synthesized compounds, were found to have moderate effect on Aspergillus flavs fungi, specially compound [3], in comparison with antifungal treatments.
Sixth: All synthesized compounds, were found to have moderate effect on Pencillnium fungi, specially compound [3, 4], in comparison with antifungal treatments.

Table 2: Antimicrobial activity of compounds [1-11]

No.	Structure of compounds	Mean of Inhibition zone Diameter (mm)					
		Staphylococcus aurous	Bacillus	Escherichia coli	Klebsiella pneumonia	Aspergillus flavs	Peneicllium
1		23	30	8	10	11	13
1a		9	17	15	10	11	14
1b		15	-	23	8	9	10
2		20	17	8	12	12	-
2a		15	14	14	10	10	12
2b		8	13	31	8	11	10
3		20	11	14	18	20	17
4		13	9	8	8	10	17
4a		14	11	12	16	12	10
4b		13	12	12	18	12	10
5	Cephalexin	18	5	-	-	-	-
6	Amoxicillin	12	7	-	-	-	-
7	Tetracycline	7	-	10	12	-	-
8	Lincomycine	-	-	22	20	-	-
9	Nystatine	-	-	-	-	17	20
10	Fluconazole	-	-	-	-	12	15
11	Dimethyl sulphoxide	0.0	0.0	0.0	0.0	0.0	0.0

References

[1] H.M.F. Madkour. Reactivity of 4H-3, 1-benzoxazin-4-ones towards nitrogen and carbon nucleophilic reagent applications to the synthesis of new heterocycles. Arkivoc 2004 (i) 36-54.

[2] Akhil A. Nagar, Ashish Patel, Rajesh K.S, Kishore R. Danao, L.G. Rathi. Solvent Free One Pot Microwave Synthesis of Quinazolin 4- (3H) -One Derivatives with their Antibacterial and Antifungal Activity. Pharmagene Vol: 1, Issue: 1,. 2013: 1-6.

[3] Daniel L, Lednicer G, Lester A, et al. The Organic Chemistry of Drug Synthesis, Wiley Interscience Publication, New York, 1980; 2:361.

[4] Kashaw S, and Stables JP, Synthesis and CNS depressant activity of some derivatives of novel 3-[5-substituted-1, 3, 4-thiadiazole-2-yl]-2-styryl quinazolin-4- (3H) -one. Eur. J. Med. Chem., 2007; xx:1-7.

[5] AAF. Wasfy, OA. Fathalla, AA. Salman. design, synthesis and biological evaluation of novel quinazoline derivatives as potential anticancer agent, IJRPC 2014, 4 (3), 501-508.

[6] Abouzid K and Shouman S. Design, synthesis and in vitro antitumor activity of 4-aminoquinoline and aminoquinazoline derivatives targeting EGFR tyrosine kinase. Bioorg and Med, Chem. 2008;16:7543–7551.

[7] Alagarsamy V, Salomon VR, Vanikavitha G, Paluchamy V, Chandran, MR, Sujin AA, Thangathiruppathy A, Amuthalakshmi S and Revathi R. Synthesis, analgesic, anti-inflammatory and antibacterial activities of some

novel 2-phenyl-3-substituted quinazolin-4 (3H) ones. Bio pharma Bult. 2002;25 (11):1432-1435.
[8] Berger M, Albrecht B, Berces A, Ettmayer P, Neruda W and Woisetschl M. ager, S (+) -4- (1 phenylethylamino) quinazolines as inhibitors of human immunoglobuline E synthesis: potency is dictated by stereochemistry and atomic point charges at N-1.J Med chem. 2001;44:3031–3038.
[9] Chandrika PM, Yakaiah T and Narsaiah. B. Synthesis leading to novel 2, 4, 6- trisubstituted quinazoline derivatives, their antibacterial and cytotoxic activity against thp-1, hl-60 and a375 cell lines. Indian J chem. 2009;48:840–847.
[10] Cohen MH, Williams GA, Sridhara R, Chen G and McGuinn WD. Jr. United States Food and Drug Administration Drug Approval summary: Gefitinib (ZD1839; Iressa) tablets. Clin Cancer Res. 2004;10:1212-1218.
[11] El-Farargy AF, Hamed MM and Said SA. Some Reaction of 4- Chloro, 4-hydazino-2- (α-Naphthylmethyl) -Quinazoline. Egypt J Chem.1993;36 (6):497.
[12] Fathalla OA, Kassem EMM, Kamel MM and Mohamed NA. Synthesis of Some New 2-[(E) -2-furan-2-yl-vinyl]-3Hquinazolin-4-one derivatives of expected biological ical Activity. Egypt J Chem. 2009;52:573-584.
[13] Desai NC, Shah BR and Patel HH, anti HIV-1 activity of n- substituted aryl acetamides, Ind. J. of Chem, 1995;34B:201-208.
[14] Madkour, H.M.F.; Mahmoud, M.R.; Nassar, M.H.; Habashy, M.M. Sulfur Lett. 1998, 21, 253.
[15] Madkour, H.M.F.; Salem, M.A.I.; Abdel-Rahman, T.M.; Azab, M.E. Heterocycles 1994, 38, 57.
[16] AAF. Wasfy, NA. Mohmed AA. Salman. synthesis and anti-cancer properties of novel quinazoline derivatives. IJRPC 2015, 5 (1), 34-40.
[17] Amin KM, Kamel MM and Anwar MM. Eur J Med Chem. 2010;45 (2):117–2131.
[18] Alagarsamy V, Raja, Solomon V and Dhanabal K. Bioorg Med Chem.2007;15:235–241.
[19] Vijaynathappa J and Bhojraj S. Journal of health sciences. 2008;54:524-528.
[20] Al-Obaid AM, Abdel-Hamide SG and El-Kashef HA. Eur J Med Chem. 2009;44:2379–2391.
[21] Chandregowda V, Kush AK and Chandrasekara G. Eur JMed Chem. 2009;44:3046-55.
[22] Giri RS, Thaker HM and Giordano T. Bioorg Med Chem. 2010;18:2796– 2808.
[23] Qian L, Shen Y and Chen J. Acta Phys Chim Sin. 2006;22:1372−1376.
[24] Ashraf A, Khalil, Sami, Abdel Hamide G, Abdulrahman, Al-Obaid M, Hussein and El-Subbagh I. Arch Pharm Pharm Med Chem. 2003;2:95–103.
[25] Guan J, Zhang Q, O'Neil M, Obaldia N, Ager A, Gerena L and Lin AJ. Antimicrob Agents Chemother.2005;49 (12):4928-33.
[26] Ilango K, Valentina P, Umarani N, Beena K.P. Eco-benign mediated versatile synthesis of newer quinazolin-4- (3H) -one clubbed isatin derivatives as potent antimicrobial agents. Int. J. Res. Pharm. Sci. Vol-1, Issue-2, 133-138, 2010.
[27] AAF Wasfy, Synthesis and antimicrobial evaluation of some 2, 2-disubstituted-3, 3- biquinazolin-4- (3H) -ones. Indian Journal of Chemistry, 2003, 3102-3107.
[28] Ashok Kumar, Chatrasal singh Rajput, Synthesis and anti-inflammatory activity of newer quinazolin-4-one derivatives. European Journal of Medicinal chemistry, 2009, 83-90.
[29] Ashok kumar, Mirdula Tyagi, Srivastava V.K., Newer Potential quinazolinones as hypotensive agents. In-dian Journal of Chemistry, 2003, 2142-2145.
[30] Fawzia M Refaie, Amry Esmat, The antihyperlipidemic activities of 4- (3H) -quinazolinones and two halogented derivatives in rats. Lipid in health and disease, 2005, 22.
[31] Rajiv dahiya, Anilkumar, Synthesis and biological activity of peptide derivatives of Iodoquinazolonones. Mo-lecules, 2008, 958-976.
[32] Surendranath Pandeya, Raja A.S., Nath G., Synthesis and antimicrobial evaluation of some 4 or 6- chloro isatin derivatives. Indian Journal of Chemistry, 2006, 494-499.
[33] Buyuktimkin S., Ekinici A.C., Pharmacological studies on quarternized–4- (3H) - quinazolinones. Journal of Pharmaceutical sciences, 2006, 1092 – 1094.
[34] Abdallah A. El-Sawya, Shaaban K. Mohamedb*, Abd El-Monem M. F. Eissaa, Ahmed H.Tantawya, Yvette A. Issaca. Synthesis, reactions and biological evaluation of pentadecanyl benzoxazinone and pentadecanyl quinazolinone derivatives. J. Chem. Pharm. Res., 2012, 4 (5):2755-2762.
[35] Sharma GVR, Alice R Robert, Devi B. A Formal and Simple Synthesis of an Antifungal Quinazolinone of Marine Source. Nat Prod Chem Res 2014, 2:4.
[36] Xu Z, Zhang Y, Fu H, Zhong H, Hong K, et al. (2011) Antifungal quinazolinones from marine-derived Bacillus cereus and their preparation. Bioorg Med Chem Lett 21: 4005-4007.
[37] Duan Y, Zhu XY, Ma JA, Zhou YG (2013) Palladium-catalyzed asymmetric hydrogenation of fluorinated quinazolinones. Tetrahedron Letters 54: 6161-6163.
[38] Zakaria H. Aiube, Zainab A. Jabarah,. Design-Syntheses, Characterization and Biological Activity Studies of Azobenzen-P, P'-Di (3, 1-Benzoxazin-4-One-2yl) and Azobenzen-P, P'-Di[(3-Substituted-3 (4H) Quinazolinone-Chem Sci J, Volume 8. Issue2. 2017. 1000156.
[39] Ern¨o P., Philippe B., Martin B.; Structure determination of organic compounds, 4th, 2009, pp 443.

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