ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 3| March 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL EVALUATION OF SOME NEW 4(3H)-QUINAZOLINONE

Pankaj Kumar, Arun Patel, Shailendra Patel
Shri Ram Group of Institutions, Faculty of Pharmacy, Jabalpur (M.P.), India

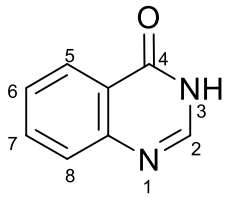
ABSTRACT

Heterocyclic systems comprising quinazolinones have been explored to a major extent in last few decades due to its chemotherapeutic and antimicrobial potential. Quinazolinone is a bicyclic compound containing benzene ring fused with pyrimidine ring. Microbiology is the study of microscopic organisms such as bacteria, viruses, fungi and protozoa. This discipline includes fundamental research on the biochemistry, physiology, cell biology, ecology, evolution and clinical aspects of microorganisms, including the host response to these agents. Bacterial resistance to existing drugs is a growing problem in the world. The antibacterial and antifungal activity data of 2,3-disubstituted 4(3H)-quinazolinone derivatives (6A-6J) indicated that the compounds have significant inhibitory activity on all the bacterial and fungal strains at both 50 µg (0.05 ml) and 100 µg (0.1 ml) dose levels when compared with standard. Among all the compounds tested, compounds 6A, 6B, 6C and 6D possessed maximum activity in both fungal as well as bacterial strains. These compounds possessed the halogens on the aromatic ring and thus reveal the positive contribution of electron withdrawing groups to the antibacterial activity.

INTRODUCTION

The word 'drug' is derived from the French word drogue, which means a dry herb. In a general way, a drug may be defined as a substance used in prevention, diagnosis, treatment or cure of disease in man or animals. Fighting diseases with drugs is the timeless struggle [1]. So are the search drugs to combat them. In the earliest days of civilization man was totally dependent on nature not only for food but also for treatment of various diseases. He used the plants around him for treating ailments. At a time thousands of acres of land is required for growing plants such as Indigo and Turkey red. Organic chemical research showed how to synthesize these dyes from coal-tar and thus released this land for other productive uses. In many cases the synthetic materials are superior to the natural compound e.g. synthetic dyes are superior to those obtains from natural origin. In other case, the synthetic materials are entirely unknown in nature and fill the requirements not satisfied from any other source [2]. Examples are ether, glycol, aspirin, and sulpha drugs. Synthetic organic chemistry touches almost every phase of life.

Heterocyclic compound can be aliphatic or aromatic in character depending upon the electronic constitution. The atoms of a simple heterocyclic ring are numbered from the heteroatom which is counted as one [5]. Substituent's are given the lowest possible numbers and then arranged in alphabetical order viz. quinazolinone the nucleus of present study is numbered as follows:



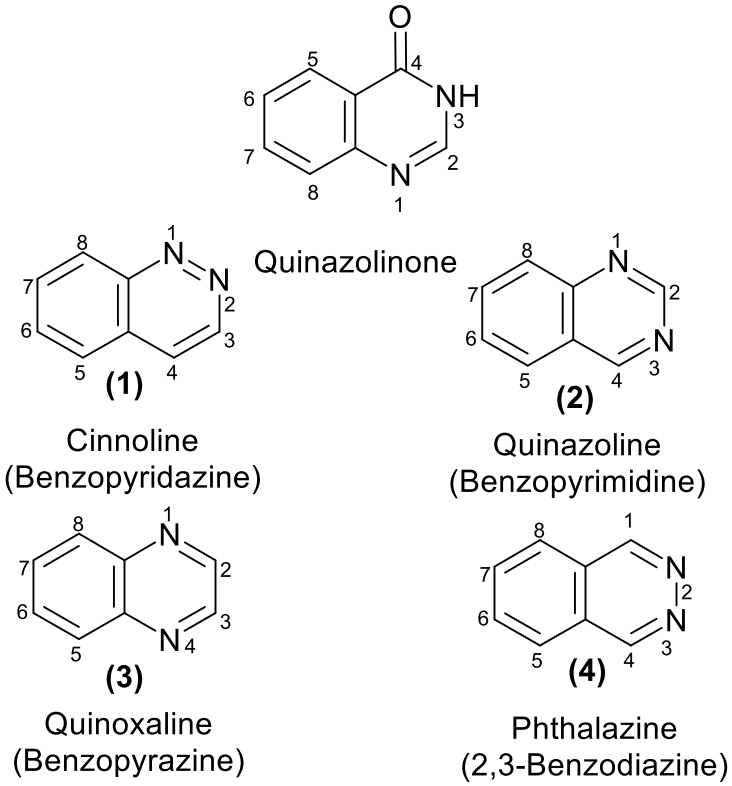
Quinazolinone

Quinazolin-4(3H)-one is a versatile pharmacophor which exhibits wide variety of biological activities like hypnotic, antitussive, analgesic, muscle relaxant, anticonvulsant, antiallergic, antibacterial, hypoglycemic and antispasmodic [6-10].

An important quinazolin-4(3H)-one is 2-methyl-3-0-tolyl-4(3H)-quinazolinone known as methaqualone[11] is a potent sedative-hypnotic (non-barbiturate) introduced in 1965. The marketed product of this quinazolinone in U.S.A. is Quaalude(R), iparset(R) and sopor(R) in the form of HCl salt.

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 3| March 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

Quinazoline is a compound in which pyrimidine fused with benzene and is called benzopyrimidine.Since N^+ and C are isoelectronic, the simplest and most direct hetero analogue of benzene is the pyrimidinium ion. There are several examples of benzene fused with six membered ring containing two nitrogen atoms. Some of the examples are benzodiazines (cinnoline, phthalazine, quinoxaline, quinazoline). Quinazoline or benzopyrimidine is the fused pyrimidine with benzene[12].



Depending upon the position of the keto or oxo group, Quinazolinone compounds may be classified into two types: 2-(1H)quinazolinone or 1,2-dihydro-2-oxoquinazolines and 4(3H)-quinazolines or 3,4-dihydro oxoquinazolines. These system exhibit lactam-lactim tautomerism and undergo hydroxy group replacement reactions.

Worldwide literature survey indicates that infectious diseases can be cured using the traditional system of medication which is highly acknowledged and considered to be one of the primary systems of healthcare management. Prehistoric pieces of evidence from the age of Neanderthal men, historical documentation of ancient civilizations, age-old practices of ethnomedicine and modern clinical research all have represented the curative potential of plants in the form of extracts or other alternative forms of medical treatments [28].

Throughout the globe, natural therapeutics came into demand in the late 1990s and eventually opened a new branch of research, entitled as complementary and alternative medicine (CAM) with lesser side effects, broad-spectrum activity against a number of ailments, high tolerability, low toxicity level, lower cost and great enough pharmacokinetics to be clinically effective without chemical change and/or alteration [29].

Currently, more than 80% of the world's population is significantly relying on conventional plant based pharmaceutical products as therapeutics to address a wide array of human medical conditions [30]. Undoubtedly, the interest in searching new drugs from plant source has been tremendously increasing among researchers around the globe. Several plant secondary metabolites for example flavonoids, tannins, alkaloids, anthocynidin glycosides, essential oils, and terpenoids, have been reported to have significant antimicrobial activity [31]. Several research groups from various parts of the world have reported that various plant species possessing significant antimicrobial properties [32] through in- silico, in-vitro and/or in-vivo experimental settings [33].

Undoubtedly antibiotic drug resistance (ADR) and/or antimicrobial resistance (AMR) is accepted as one of the major challenges of the 21st century by every apex economic, political and regulatory bodies including the International Monetary Fund (IMF), the World Bank (WB), the World Health Organization (WHO), and the Group of Eight (G8). AMR imposes the greatest major problems and challenges

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 3| March 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

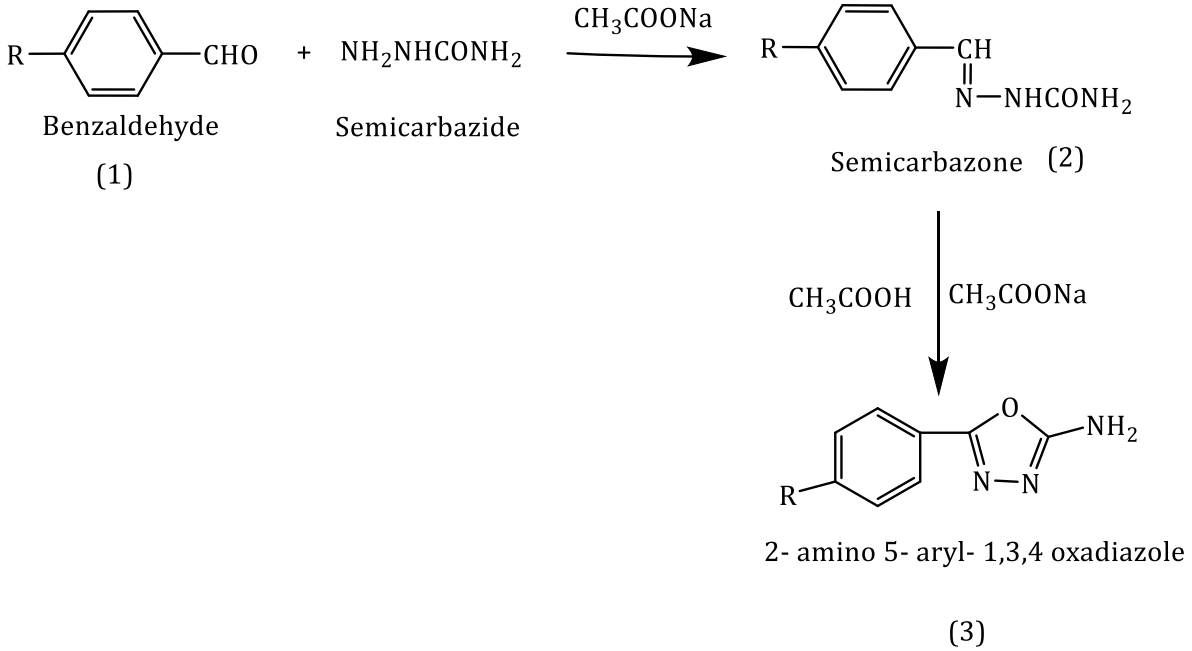
to the public health threat (chemotherapeutic failure), social, animal health and environmental concern/crises imposing a serious real global issue [34].

Therefore, the AMR problem is presently viewed by two parallel holistic and multidisciplinary principles, One Health and Global Health, which were used in general to address problems associated with infectious disease, and AMR in particular. According to new figures, the number of people that die each year because of AR infections or AMR is approximately 700,000 and it is anticipated that it will spike to 10 million people each year by 2050 at a global scale [35]. This relationship indicates that public health and animal health are mutually dependent on each other and the environment in which they live in particular.

The antibiotic resistance (AR) motivated the researchers and biopharmaceutical industries to come up with new classes of antibiotics. However, there has been a rapid decline in the global funding and investment for research to the advancement of novel antibiotics by the growing biotechnology industry and pharmaceutical companies and government guidelines and regulations impacting the speed of translational research [36]. Decision-makers, regulators and many organizations accept the global public health consequences of a deteriorating antibiotic drug discovery and development pipeline. However, with an expected rejection rate of 95% [37]. it is a known fact that it is a very challenging and tedious task to develop a new antibiotic. Moreover, new antibiotic development costs billions of US dollars.

MATERIALS AND METHODS
SCHEME FOR SYNTHESIS

(a) Synthesis of 2-amino-5-arylsubstituted-1,3,4–oxadiazole



Benzaldehyde (1)

Semicarbazide

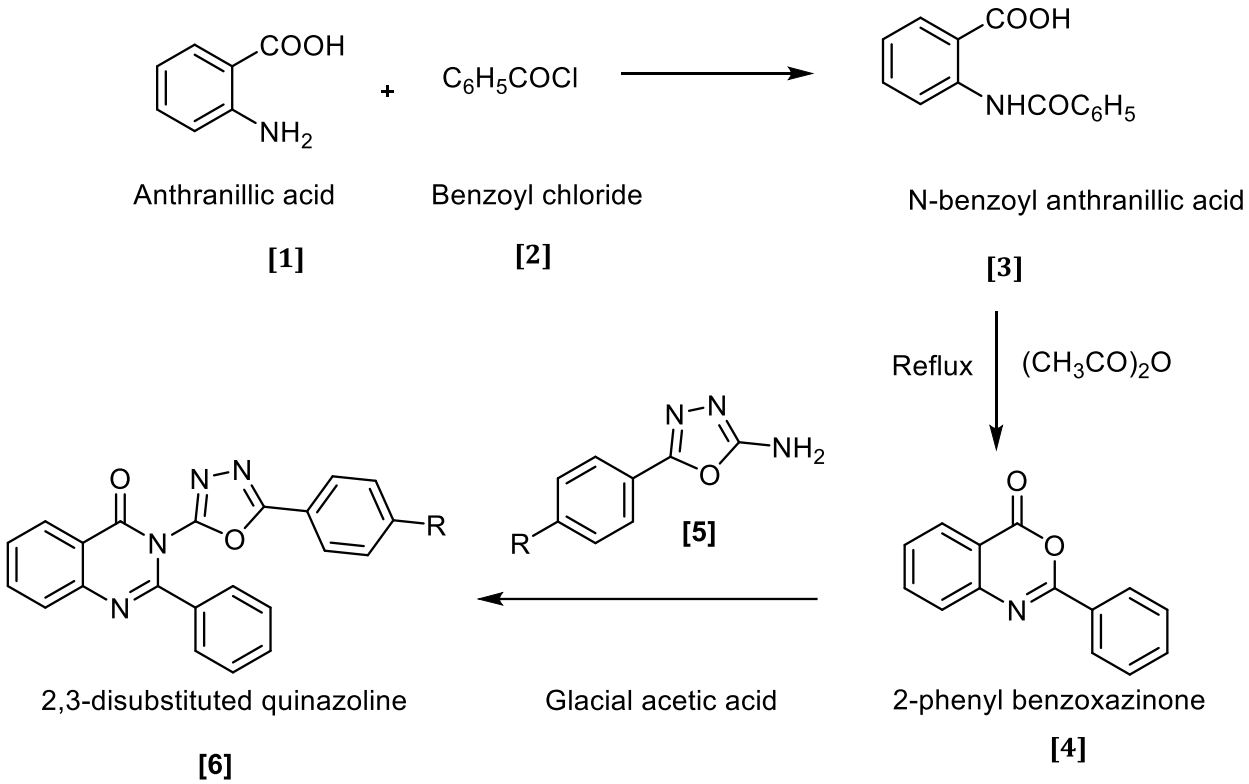
Semicarbazone (2)

2- amino 5- aryl- 1,3,4 oxadiazole

(3)

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 3| March 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

(b) Synthesis scheme of title compounds (2,3-disubstituted quinazoline)



The synthesized compounds are

Compound 6A: 3-(5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl)-2-phenylquinazolin-4(3H)-one

Compound 6B: 3-(5-(4-bromophenyl)-1,3,4-oxadiazol-2-yl)-2-phenylquinazolin-4(3H)-one

Compound 6C: 3-(5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl)-2-phenylquinazolin-4(3H)-one

Compound 6D: 2-phenyl-3-(5-(p-tolyl)-1,3,4-oxadiazol-2-yl)quinazolin-4(3H)-one

Compound 6E: 3-(5-(4-methoxyphenyl)-1,3,4-oxadiazol-2-yl)-2-phenylquinazolin-4(3H)-one

Compound 6F: 3-(5-(4-ethylphenyl)-1,3,4-oxadiazol-2-yl)-2-phenylquinazolin-4(3H)-one

Compound 6G: 3-(5-(4-ethoxyphenyl)-1,3,4-oxadiazol-2-yl)-2-phenylquinazolin-4(3H)-one

Compound 6H: 3-(5-(2-chlorophenyl)-1,3,4-oxadiazol-2-yl)-2-phenylquinazolin-4(3H)-one

Compound 6I: 3-(5-(2-bromophenyl)-1,3,4-oxadiazol-2-yl)-2-phenylquinazolin-4(3H)-one

Compound 6J: 3-(5-(2-nitrophenyl)-1,3,4-oxadiazol-2-yl)-2-phenylquinazolin-4(3H)-one

All the compounds were synthesized with good yields and purity. The compounds were characterized by subjecting to various spectral studies such as IR and ^{1}H NMRetc.

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 3| March 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

PHYSICO-CHEMICAL CHARACTERIZATION

Physical parameters of the compounds

Comp.	Mol. Formula	Mol. wt.	% Yield	Physical Appearance		Melting Point (˚C)	R_f value
				Color	State		
6A	$C_{22}H_{13}ClN_4O_2$	400.82	76	Shiny white	**Solid**	270-272°C	
6B	$C_{22}H_{13}BrN_4O_2$	445.28	56	Off white	**Solid**	243-245°C	
6C	$C_{22}H_{13}N_5O_4$	411.38	78	Yellow	**Solid**	260-262°C	
6D	$C_{23}H_{16}N_4O_2$	380.41	70	Cream	**Solid**	176-178°C	
6E	$C_{23}H_{16}N_4O_3$	396.41	68	Cream	**Solid**	166-268°C	
6F	$C_{24}H_{18}N_4O_2$	394.43	65	Light brown	**Solid**	233-235°C	
6G	$C_{24}H_{18}N_4O_3$	410.43	62	Off grey	**Solid**	213-215°C	
6H	$C_{22}H_{13}ClN_4O_2$	400.82	55	Shiny white	**Solid**	255-257°C	
6I	$C_{22}H_{13}BrN_4O_2$	445.28	48	Yellow	**Solid**	248-250°C	
6J	$C_{22}H_{13}N_5O_4$	411.38	68	Off white	**Solid**	250-252°C	

6.3 Solubility studies of the synthesized compounds

Compound	Water	Alcohol	Acetone	Glacial Acetic Acid	Benzene	Dimethyl Sulfoxide
6A	-	+++	+	++	-	++
6B	-	+++	+	++	-	++
6C	-	+++	+	++	-	++
6D	-	+++	+	++	-	++
6E	-	+++	+	++	-	++
6F	-	+++	+	++	-	++
6G	-	+++	+	++	-	++
6H	-	+++	+	++	-	++
6I	-	+++	+	++	-	++
6J	-	+++	+	++	-	++

- Insoluble; + = Slightly soluble; ++ = soluble; +++ = Freely soluble

Agar Diffusion Method

This method gives the extent of growth of the microorganism, inoculated into a solid nutrient agar bed by the antimicrobial substance. The test substance is kept in a cup made of agar bed, diffuses into it and inhibits the growth of microorganism. The diameter of the zone of inhibition is measured in comparison with suitable drug substance, is considered as potency of that substance. The diameter of zone of inhibition is directly proportional to the concentration of the drug substances added into the cup, thickness of the agar bed, diffusion coefficient of the antimicrobial substance into the agar cup, sensitivity of the microorganism to the test substance and the temperature. The appropriate media is sterilized and cooled to 42°C, incubated with the test organism, mixed uniformly and poured into petri plates and cooled. Bores are made into it; specified test solution is added and left at room temperature for 30 min. Incubate at 37°C for 24 hrs. The zone of inhibition is measured in mm [29].

Antibacterial screening of the synthesized compounds

For the anti-bacterial screening of the synthesized compounds the two gram-negativebacterial species were taken and enlisted in Table 5.1.

Table 1: List of Bacterial strains

S. No.	Microbial strains	MTCC No.*	Strain (Gram +/-)	Incubation Temp.	Incubation period
1.	*Pseudomonas Aeruginosa*	424	-ve	37	24h
2.	*Escherichia Coli*	40	-ve	37	24h

*****Procured from IMTECH Chandigarh.

Antibacterial Activity

The synthesized 2,3-disubsituted 4(3H) quinazolinone derivatives were screened for the antibacterialactivity against two Gram-negative bacteria viz.,*Escherichiacoli* and*Pseudomonasaeruginosa* by using the Agar diffusion method**.** Ciprofloxacinwas used as reference standard forcomparing the synthesized compounds for its efficacy.

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 3| March 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

Culture medium: Nutrient broth was used for the preparation of inoculum of the bacteria and nutrient agar was used for the screening method.

Composition of Nutrient Agar Medium

a) Peptone 5.0 gm
b) Sodium chloride 5.0 gm
c) Beef extract 1.5 gm
d) Yeast extract 1.5 gm
e) Agar 15.0 gm
f) Distilled water (q.s) 1000 ml
g) pH (7.4±0.2)

The test organisms were subcultured using nutrient agarmedium. The tubes containing sterilized medium were inoculated with the respective bacterial strain. After incubation at 37ºC ±1ºC for 18 hours, they were stored in a refrigerator. The nutrient agar mediumwas sterilized by autoclaving at 121ºC (15 lb/sq.inch) for 15 min. The petriplates, tubes and flasks plugged with cotton were sterilized in hot-air oven at 160ºC, for an hour. Into each sterilized petriplate (20 cm diameter), was poured about 125ml of molten nutrient agar medium which was already inoculated with the respective strain ofbacteria (5 ml of inoculum to 250 ml of nutrient agar medium)aseptically. The plates were left at room temperature aseptically to allow the solidification. After solidification, the cups of each of 7 mm diameter were made by scooping out medium with a sterilized cork borer from a petridish and labeled accordingly.

Antifungal screening of the Synthesized Compounds

For antifungal screening the following fungal species were used (Table 5.2).

Table 2: List of Fungal Strains

S. No.	Fungal strain	MTCC* No.	Incubation Temperature (ºC)	Incubation period
1.	*Aspergillus Niger*	281	25	5 days
2.	*Candida albicans*	227	25	2 days

*Procured from IMTECH Chandigarh.

RESULT AND DISCUSSION

Antibacterial Activity

In accordance with the data obtained from antibacterial activity, all the synthesized 2,3-disubstitued 4(3H)-quinazolinone (6A-6J) have showed activity against testedorganisms. Antibacterial activity of the synthesized compounds has been carried outfor gram-negative bacterial strain.

Antibacterial Activity Against Gram Negative Bacteria

The Data of antibacterial activity against the gram- negative bacterial strains (*Escherichia Coli*and*Pseudomonasaeruginosa*) suggested the order of activity of compounds: 6A > 6C> 6B > 6D > 6F > 6E > 6G> 6H> 6J > 6I.

Antibacterial activity of synthesized 2,3-disubstitued 4(3H) quinazolinone derivatives against gram negative bacteria.

S. No.	COMPOUND	Zone of inhibition in mm			
		Pseudomonas Aeruginosa		*Escherichia coli*	
		50µg	100µg	50µg	100µg
1.	6A	19.05±0.21	22.11±0.25	18.07±0.26	20.02±0.21
2.	6B	16.28±0.28	19.24±0.25	15.32±0.27	18.25±0.28
3.	6C	18.28±0.24	21.28±0.28	17.30±0.22	19.25±0.24
4.	6D	14.05±0.24	16.10±0.22	13.09±0.23	15.02±0.24
5.	6E	12.57±0.26	14.59±0.23	11.61±0.27	13.54±0.28
6.	6F	13.57±0.25	15.54±0.26	12.56±0.23	14.54±0.23
7.	6G	11.67±0.24	12.64±0.29	10.71±0.23	12.64±0.24
8.	6H	08.45±0.23	10.46±0.26	07.49±0.22	09.42±0.23
9.	6I	07.15±0.27	09.19±0.27	06.19±0.27	08.12±0.22
10.	6J	09.31±0.23	09.52±0.23	07.35±0.25	09.28±0.22
11.	Ciprofloxacin	19.28±0.36	23.45±0.23	19.70±0.65	22.65±0.26

The order of activity of synthesized compound is:6A > 6C> 6B > 6D > 6F > 6E > 6G> 6H> 6J > 6I

Compounds 6A (18.07±0.26),6B (15.32±0.27), 6C (17.30±0.22), 6D (13.09±0.23), 6E (11.61±0.27), 6F (12.56±0.23) 6G (10.71±0.23), 6H (07.49±0.22), 6I (6.19±0.27) and 6J (07.35±0.23)has shown zone of inhibition (mm) in comparison to standard drug (Ciprofloxacin, 19.70±0.65) has shown good activity against *Escherichia coli* (gram negative bacteria) at 50µg concentration.

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 3| March 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

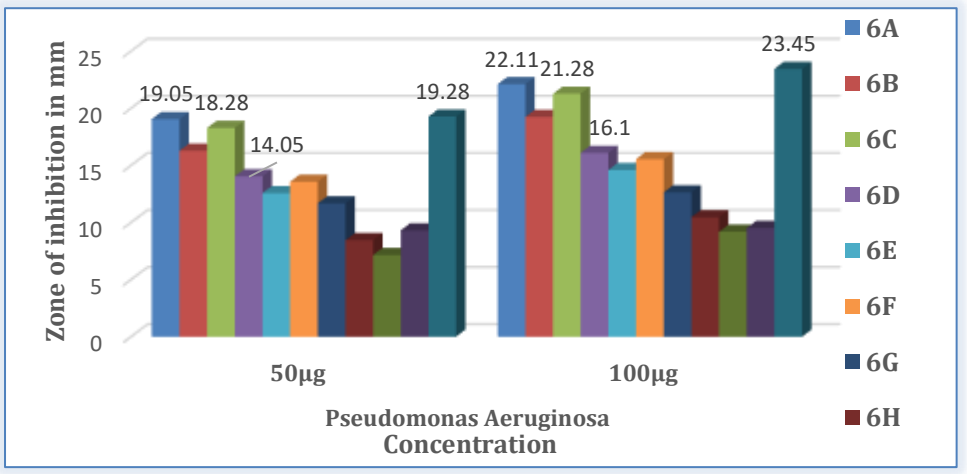


Figure 1: Graph showing Zone of inhibition of the synthesized derivatives against gram negative bacteria.

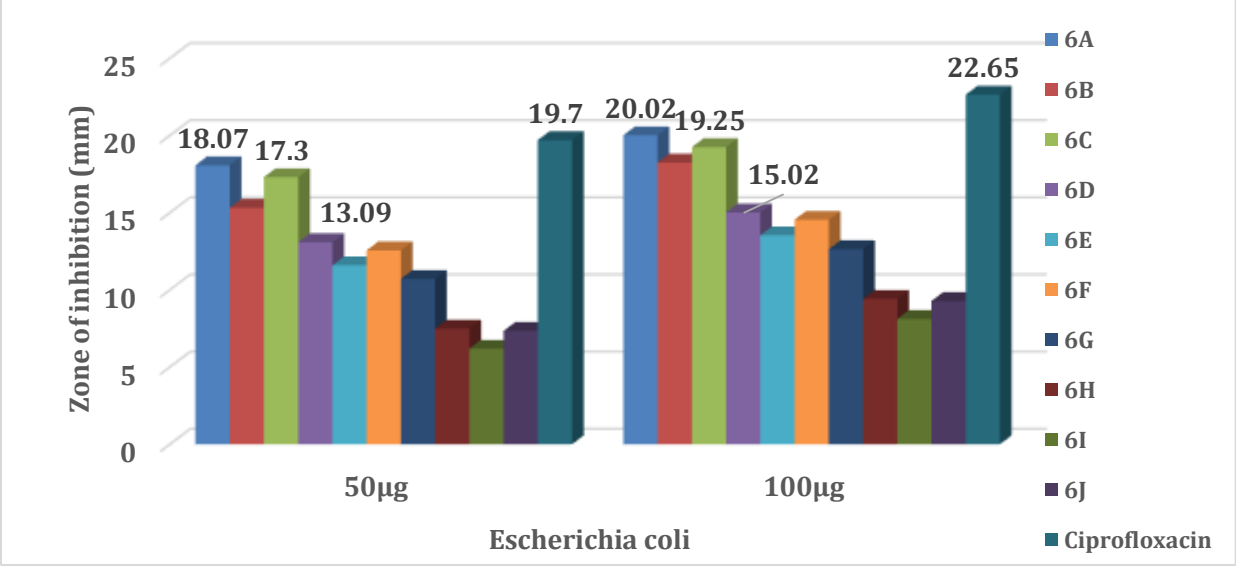


Figure 4: Graph showing Zone of inhibition of the synthesized derivatives against gram negative bacteria.

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 3| March 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

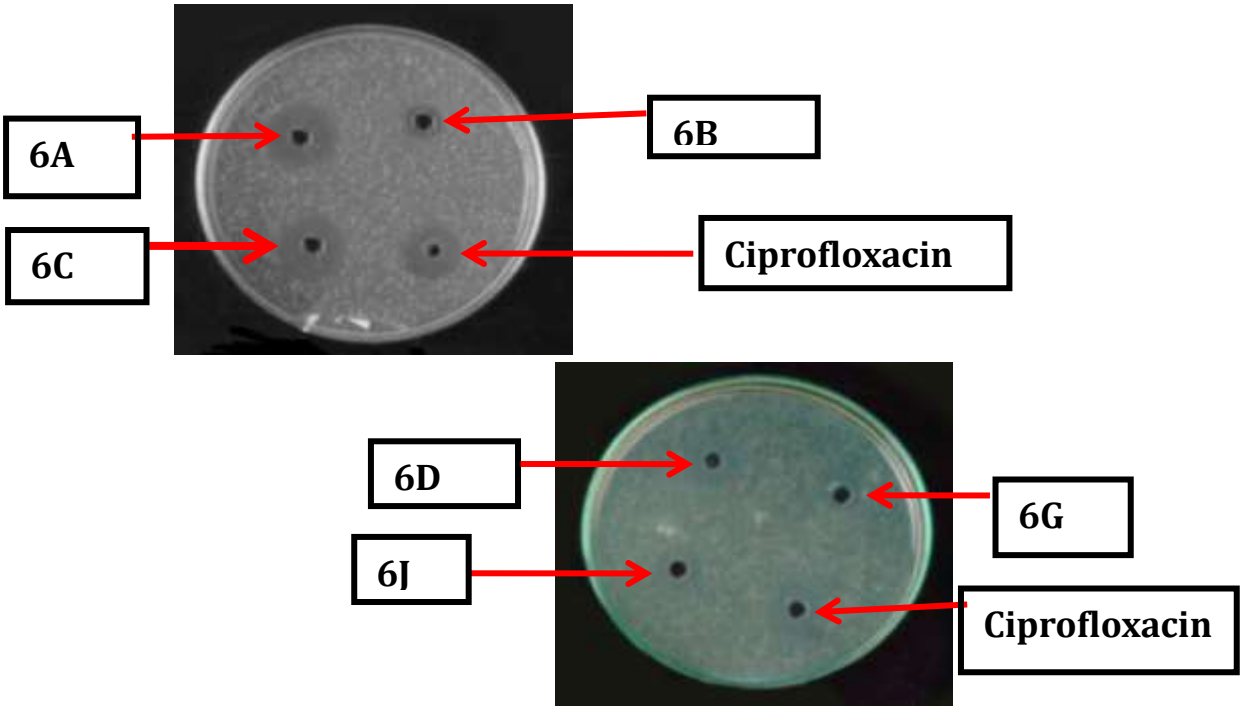


Figure 5: Zone of inhibition of synthesized derivatives against *Pseudomonas Aeruginosa*

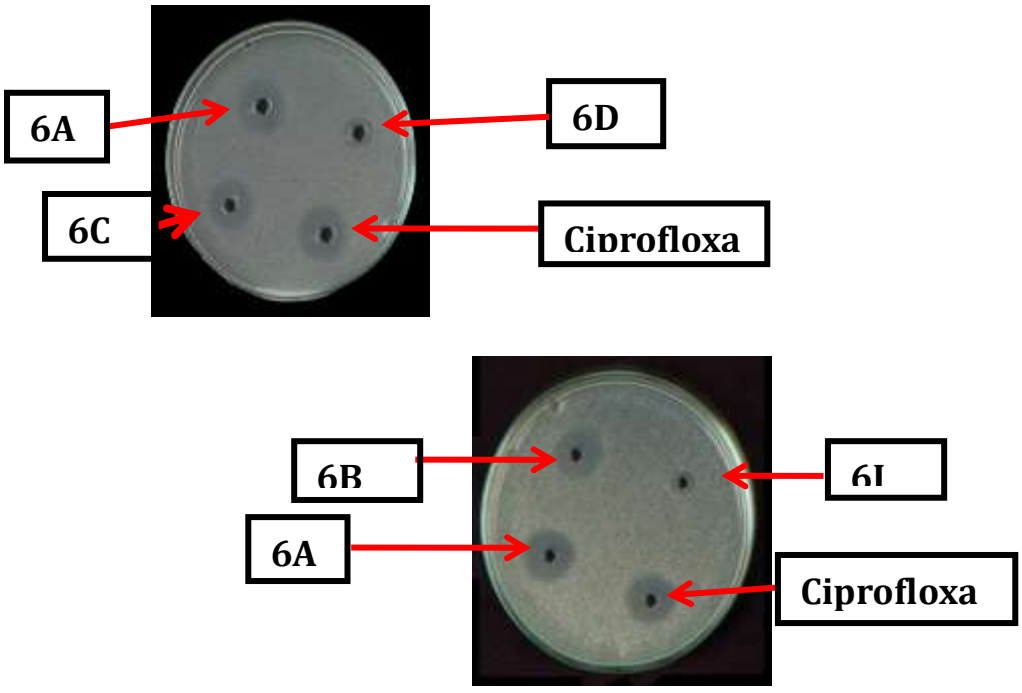


Figure 6: Zone of inhibition of synthesized derivatives against *Escherichia Coli*

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 3| March 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

Antifungal Activity of Synthesized2,3-Disubstitued 4(3H) Quinazolinone Derivatives.

COMPOUND	Zone of inhibition (mm)			
	C. Albicans		*A. Niger*	
Concentration	**50**	**100**	**50**	**100**
6A	24.75±0.53	27.65±0.43	23.34±0.28	28.25±0.32
6B	21.72±0.34	22.20±0.22	19.62±0.23	26.72±0.18
6C	22.45±0.28	26.32±0.26	22.23±0.43	26.35±0.25
6D	21.22±0.65	25.25±0.34	18.42±0.46	22.55±0.12
6E	16.42±0.67	22.72±0.27	18.52±0.25	24.32±0.14
6F	15.32±0.32	18.25±0.45	20.38±0.14	24.42±0.25
6G	14.62±0.72	17.62±0.23	17.24±0.13	22.52±0.22
6H	8.32±0.33	12.72±0.34	14.52±0.26	17.64±0.32
6I	6.32±0.84	11.12±0.25	15.65±0.12	19.22±0.14
6J	10.32±0.88	15.32±0.44	16.65±0.16	20.52±0.12
DMSO (Control)	-	-	-	-
Fluconazole	25.30 ±0.32	30.25±0.26	24.25±0.32	29.20±0.23

The order of the activity: 6A>6B>6C>6D>6E>6F>6G>6J>6H>6I

Compounds 6A (27.65±0.43),6B (22.20±0.22), 6C (26.32±0.26), 6D (25.25±0.34), 6E (22.72±0.27), 6F (18.25±0.45), 6G (17.62±0.23), 6H (12.72±0.34), 6I (11.12±0.25) and 6J (15.32±0.44)has shown zone of inhibition (mm) as compared to standard drug (Fluconazole, 30.25±0.26) has shown good activity against C. Albicans (Fungi strains) at 100 µg concentration.

However, further studies on activity and long term toxicity are to be carried out before any conclusion are drawn, as these categories of drug are known to have potential antimicrobial activity. Testing on different models can further substantiate the antimicrobial activity of the synthesized analogues. The graphical representation of antifungal activity on fungus strains was shown in Figure 5.7& 5.8 and zone of inhibition was shown in Figure 5.9 & 5.10.Antibacterial and antifungal activities of the 2,3-disubstitued 4(3H)-quinazolinone are mostly widely used and some of them are in clinical practice as antimicrobial agents. In particular 2,3-disubstitued 4(3H)-quinazolinone derivatives in recent years are extensively studied for the development of newer antimicrobial agents.

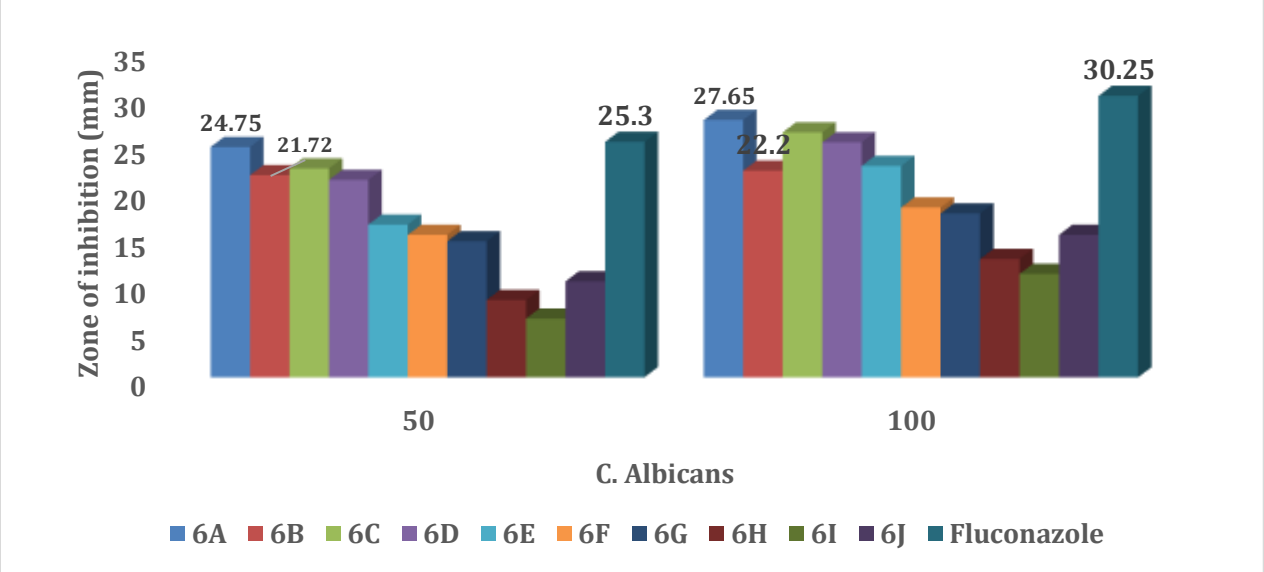


Figure 7: Graph showing Zone of inhibition of the synthesized derivatives against C. Albicans fungi.

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 3| March 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

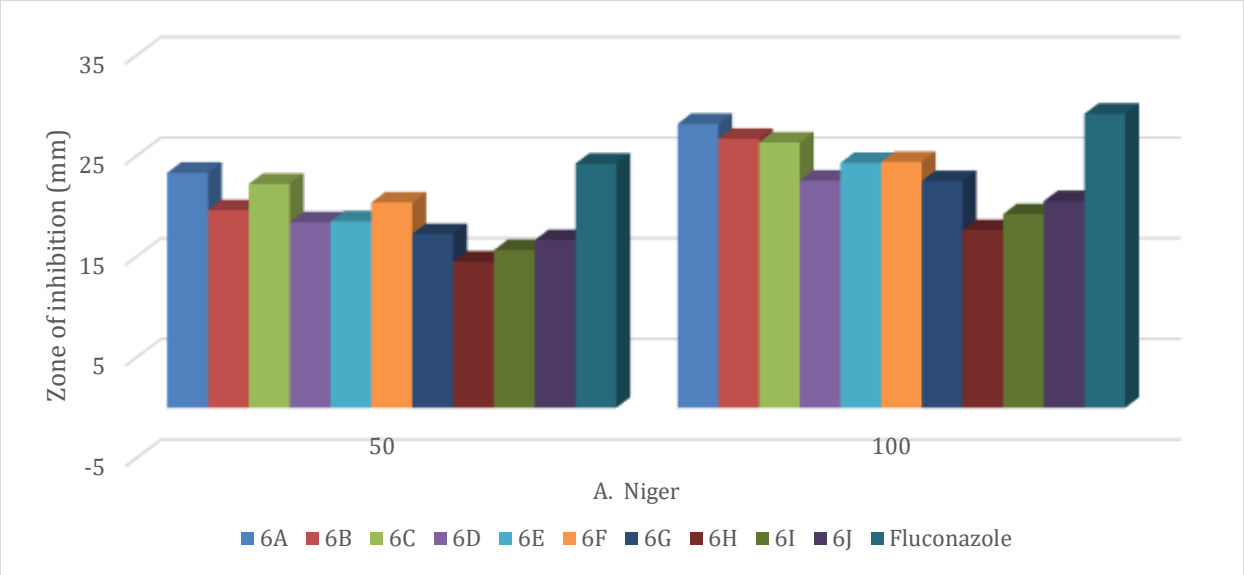


Figure 8: Graph showing Zone of inhibition of the synthesized derivatives against *A. Niger* fungi.

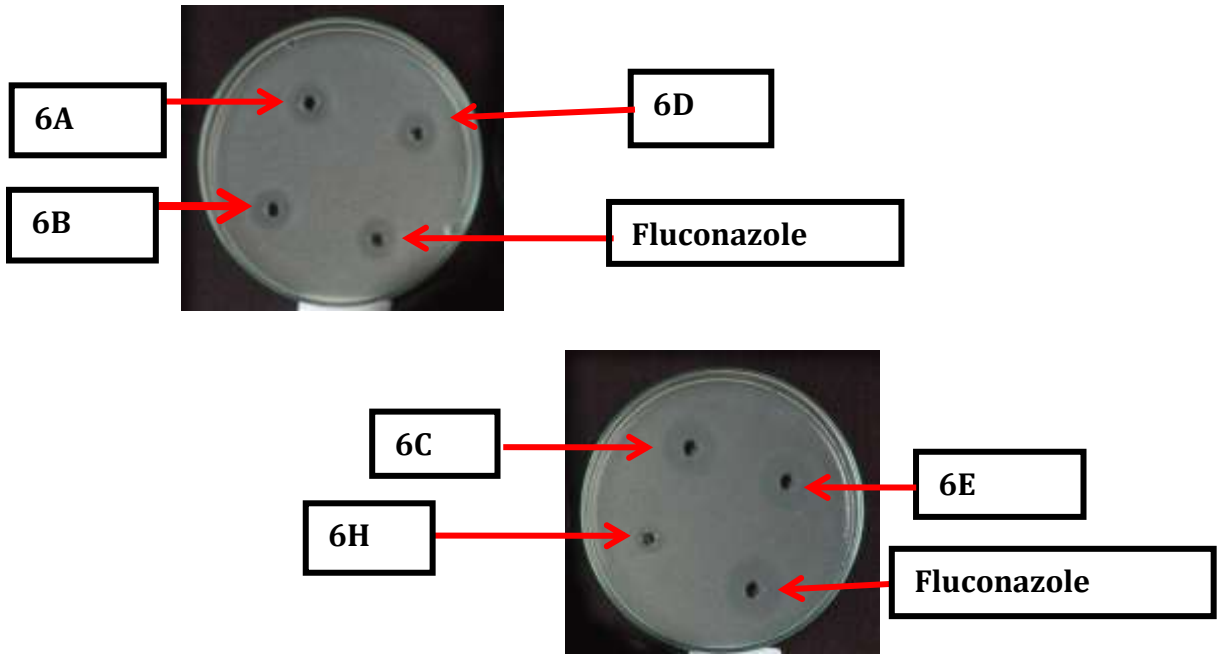


Figure 9: Zone of inhibition of synthesized derivatives against *C. Albicans*

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 3| March 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

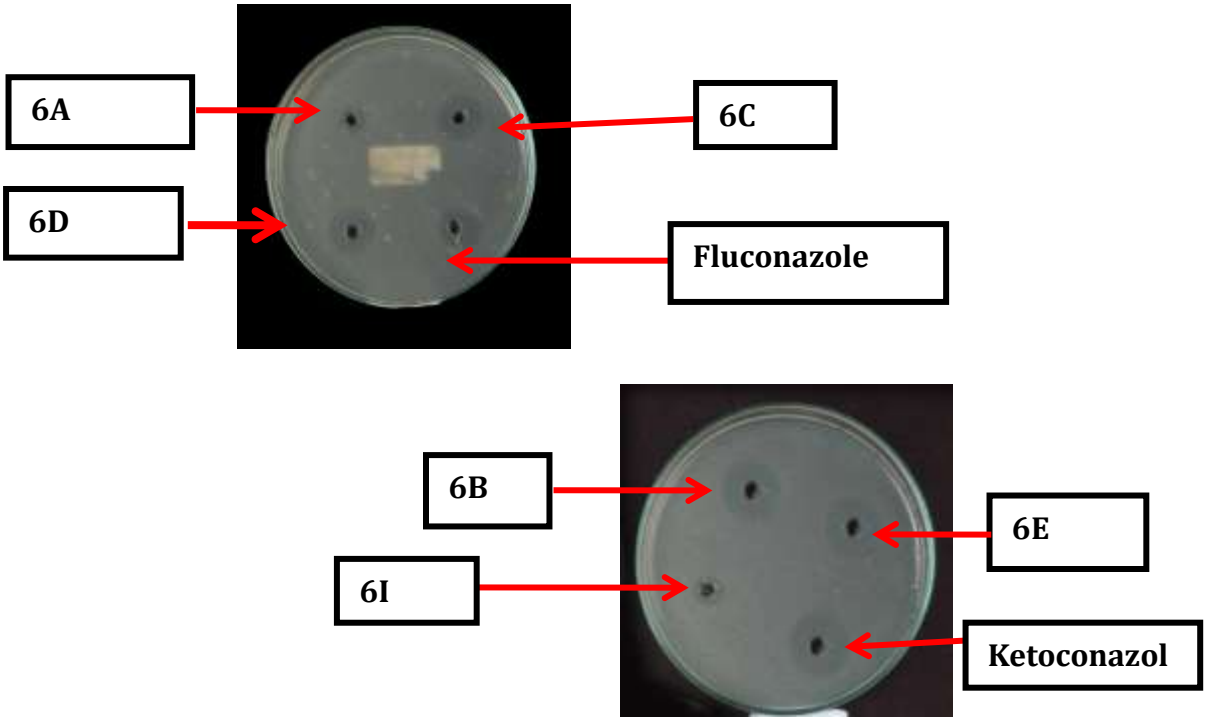


Figure 10: Zone of inhibition of synthesized derivatives against *A. Niger*

DISCUSSION AND CONCLUSION

The ten new derivatives of 2,3-disubstituted 4(3H)-quinazolinone has been prepared and evaluated for their antibacterial activity against Gram-negative bacterial strains and two fungal strains are used to carried out antifungal activity using Agar diffusion method. The Ciprofloxacin used as standard for antibacterial activity and Fluconazole was used as standard to compare the antifungal potential of the synthesized compounds.

The antibacterial and antifungal activity data of 2,3-disubstituted 4(3H)-quinazolinone derivatives (6A-6J) indicated that the compounds have significant inhibitory activity on all the bacterialand fungal strains at both 50 µg (0.05 ml) and 100 µg (0.1 ml) dose levels when compared with standard. Among all the compounds tested, compounds 6A, 6B, 6C and 6Dpossessed maximum activity in both fungal as well as bacterial strains. These compounds possessed the halogens on the aromatic ring and thus reveal the positive contribution of electron withdrawing groups to the antibacterial activity.

Presence of electronegative group (Br, Cl, and NO_2) with para substitution either at 5^{th}position along with the 1,3,5-oxadiazole at 3 position in the quinazolinone is essential for the antifungal and antibacterial activity but in case of ortho substitution may diminish the activity.

The ten new derivatives of 2,3-disubstituted 4(3H)-quinazolinone has been synthesized and characterized by IR spectrophotometric analysis and ^{1}HNMR. The synthesized compounds have shown the characteristic peaks of 3082.54 (Ar. C-H); 1766.96 (C=O str.); 1607.10 (C=N str.); 1589.64 (C-C str.); 1522.91 (C=C str.); 1250 (C-N sym. str.); 1520 (C=N str.); 1089.3 (C–O of 1,3,4-oxadiazole nucleus), 1621.2 (C=N of 1,3,4-oxadiazole nucleus), 647.0 (C-Cl), 620 (C-Br), 1493.51 (N-O asym. str.) and 1382 (sym. N=O str.). ^{1}HNMR spectrum of the synthesized compounds has shown the peaks at ppm 7.53-7.71 (2H, Ar. C-H, 1,3,4-oxadiazole); 7.49-7.78 (2H, Ar. C-H, phenyl ring); 7.68-8.13 (4H, Ar. C-H). 1.18 (3H, -CH3); 2.49-2.51 (3H, -CH_3); 3.314 (2H, -OCH_2) 3.81 (3H, -OCH3), Thin layer chromatography was performed for every individual process and has shown the Retention factor less than 0.7. These all the characterized parameter depicted that compound were synthesized as per expected and confirmed by the IR and1HNMR analysis.

The ten new derivatives of 2,3-disubstituted 4(3H)-quinazolinone has been prepared and evaluated for their antibacterial activity against Gram-negative bacterial strains and two fungal strains are used to carried out antifungal activity using Agar diffusion method. The Ciprofloxacin used as standard for antibacterial activity and Fluconazole was used as standard to compare the antifungal potential of the synthesized compounds.

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 3| March 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

The antibacterial and antifungal activity data of 2,3-disubstituted 4(3H)-quinazolinone derivatives (6A-6J) indicated that the compounds have significant inhibitory activity on all the bacterial and fungal strains at both 50 µg (0.05 ml) and 100 µg (0.1 ml) dose levels when compared with standard. Among all the compounds tested, compounds 6A, 6B, 6C and 6D possessed maximum activity in both fungal as well as bacterial strains. These compounds possessed the halogens on the aromatic ring and thus reveal the positive contribution of electron withdrawing groups to the antibacterial activity.

Presence of electronegative group (Br, Cl, and NO_2) with para substitution either at 5^{th} position along with the 1,3,5-oxadiazole at 3 position in the quinazolinone is essential for the antifungal and antibacterial activity but in case of ortho substitution may diminish the activity. The research work established the fact that 2, 3, -disubstituted quinazolinone-4-(3H) can be further studied for their variety of pharmacological activities.

REFERENCES

1. *Abbas SE, Barsoum FF, Georgey HH, Mohammed ER. Synthesis and antitumor activity of certain 2, 3, 6-trisubstituted quinazolin-4 (3H)-one derivatives. Bull Fac Pharm 2013;51:273-82.*
2. *Abbas SS, Awadallah FM, Ibrahim NA, Said EG, Kamel G. Design and synthesis of some new 3-substituted-2-[(2,4-dichlorophenoxy)-methyl]quinazolin-4(3H)-one as potential anticonvulsant agents. Journal of Medicinal Chemistry 2016;3(2): 387-392.*
3. *Abbas SY, El-Bayouki KA, Basyouni WM, Mostafa EA. New series of 4 (3H) quinazolinone derivatives: syntheses and evaluation of antitumor and antiviral activities. Medicinal Chemistry Research 2018; 27: 571-582.*
4. *Abuelizz HA, El-Dib RA, Marzouk M, Al-Salahi R. In-vitro evaluation of new2-phenoxy-benzo [g][1, 2, 4] triazolo [1, 5-a] quinazoline derivatives as antimicrobial agents Microbiology and Pathology 2018; 117 : 60-67.*
5. *Akinyele TA, Igbinosa EO, Akinpelu DA, Okoh AI. In vitro assessment of the synergism between extracts of Cocos nucifera husk and some standard antibiotics. Asian Pac J Trop Biomed 2017;7(4):306-13.*
6. *Alagarsamy V, Chitra K, Saravanan G, Raja Solomon V, Sulthana MT, Narendhar B. An overview of quinazolines: pharmacological significance and recent developments, European Journal of Medicinal Chemistry 2018; 151: 628-685*
7. *Alanazi AM, Abdel-Aziz AA, Shawer TZ, Ayyad RR, Al-Obaid AM, Al-Agamy MH, Maarouf AR, El-Azab AS. Synthesis, antitumor and antimicrobial activity of some new 6-methyl-3-phenyl-4(3H)-quinazolinone analogues: in silico studies. Journal of Enzyme Inhibition and Medicinal Chemistry 1987;31(5):721-35.*
8. *Al-Salem HS, Hegazy GH, El-Taher KE, El-Messery SM, Al-Obaid AM, El-Subbagh HI. Synthesis, anticonvulsant activity and molecular modeling study of some new hydrazine carbothioamide, benzenesulfonohydrazide, and phenacylaceto hydrazide analogues of 4(3H)-quinazolinone. Bioorganic and Medicinal Chemistry Letter 2015;25(7):1490-9.*
9. *Aly MM, Mohamed YA, El-Bayouki KA, Basyouni WM, Abbas SY. Synthesis of some new 4(3H)-quinazolinone-2-carboxaldehyde thio-semicarbazone and their metal complexes and a study on their anticonvulsant, analgesic, cytotoxic and antimicrobial activities-part-1. European Journal of Medicinal Chemistry 2010;45(8):3365-73.*
10. *Amir M, Ali I, Hassan MZ. Design and synthesis of some new quinazolin-4-(3H)-ones as anticonvulsant and antidepressant agents. Arch Pharmaceutical Research 2013;36(1): 61-8.*
11. *Arora R, Kapoor A, Gill NS, Rana AC. Quinazolinone: An overview. Int Res J Pharm 2011;2(12):21-8.*
12. *Asadia P, Khodarahmi G, Najafabadib AJ, Saghaiea L, Hassanzadeh F. Biologically active heterocyclic hybrids based on quinazolinone, benzofuran and imidazolium moieties: synthesis, characterization, cytotoxic and antibacterial evaluation. J. Heterocyclic Chemistry 2017;14: e1600411.*
13. *B. Dash, S. Dash, D. Laloo, C. Medhi, Design, synthesis and preliminary pharmacological screening (antimicrobial, analgesic and anti-inflammatory activity) of some novel quinazoline derivatives, Journal of Applied Pharma Sciences2017;7: 83-96*
14. *Banu BH, Bharathi K, Prasad KV. Synthesis, characterization and evaluation of in vitro antioxidant and anti-inflammatory activity of 2-(4-oxo-2-phenylquinazolin-3 (4H)-yl) substituted acetic acids. IOSR Journal of Pharmacy 2012; 2: 97-104.*
15. *Bartroli J, Turmo E, Alguero M, Boncompte E, Veri-cat ML, Conte L, Ramis J, Merlos M, Garcıa-Rafanell J, Forn J. New azole antifungals: Synthesis and antifungal activity of 3-substituted-4(3H)-quinazolinones. Journal of Medicinal Chemistry 2010; 41: 1869–1882.*
16. *Bengtsson-Palme J, Larsson DG. Concentrations of antibiotics predicted to select for resistant bacteria: Proposed limits for environmental regulation. Environment International 2016;86:140-9.*
17. *Chaudhary S, Singh RK, Gupta RK. Synthesis and biological activity of peptide derivatives of 2-hydroxy-5-(6-iodo-2-methyl-4-oxoquinazolin-3 (4H)-yl) benzoic acid. Asian Journal of Pharmacy and Clinical Research 2012;5:196-200*
18. *Dafale NA, Semwal UP, Rajput RK, Singh GN. Selection of appropriate analytical tools to determine the potency and bioactivity of antibiotics and antibiotic resistance. Journal of Pharmaceutical Analysis 2016;6:207-13.*
19. *Dahiya R, Kumar A (2008) Synthesis and biological activity of peptide derivatives of iodoquinazolinones/nitroimidazoles. Molecules 13: 958-976.*
20. *Dave RS, Odedara R RJ, Kalaria RI, Upadhyay JJ. Synthesis, characterization and antimicrobial activity of new quinazolin- 4(3H)-one schiff base derivatives. Journal of Chemical and Pharmaceutical Research 2012;4:4864–4869.*
21. *Desai NC, Dodiya A, Bhatt N, Kumar M. Dimeric 2-(2-chlorophenyl)-quinazolin-4-ones as potential antimicrobial agents. Medicinal Chemistry Research. 2012; 21: 1127–1135.*

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 3| March 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

22. *Desai NC, Dodiya A, Shihory N. Synthesis and antimicrobial activity of novel quinazolinonethiazolidine–quinoline compounds. Journal of Saudi Chemical Society 2013;17:259–267.*
23. *Devi K, Kachroo M. Synthesis and anti-tubercular activity of some new 2, 3-disubstituted quinazolinones. Pharmaceutical Chemistry 2014;6(5):353-9*
24. *Devi KA, Sriram MS. Synthesis and antimicrobial activity of some quinazolinones derivatives. International Journal of Drug 2012;4:324–327.*
25. *Dinari M, Gharahi F, Asadi P. Synthesis, spectroscopic characterization, antimicrobial evaluation and molecular docking study of novel triazinequinazolinone based hybrids. Journal of Molecular Structure 2018; 1156: 43-50*
26. *Dohle W, Jourdan FL, Menchon G, Prota AE, Foster PA, Mannion P, Hamel E, Thomas MP, Kasprzyk PG, Ferrandis E. Quinazolinone based anticancer agents: synthesis, antiproliferative SAR, antitubulin activity, and tubulin co-crystal structure. Journal of Medicinal Chemistry 2018; 61: 1031-1044.*
27. *EI MA, Salem MS, Al-Mabrook SAM. Synthesis and anticancer activity of novel quinazolinone and benzamide derivatives. Research in chemistry Intermediate 2018; 44: 2545-2559.*
28. *El-Azab AS, Al-Omar MA, Sayed-Ahmed MM, Abdel-Hamide SG. Design, synthesis and biological evaluation of novel quinazoline derivatives as potential antitumor agents: molecular docking study. European Journal of Medicinal Chemistry 2010; 45: 4188-4198.*
29. *El-Azab AS, Eltahir KE. Design and synthesis of novel 7-aminoquinazoline derivatives: antitumor and anticonvulsant activities. Bioorganic and Medicinal Chemistry Letter 2012;22(5):1879-85.*
30. *El-Badry YA, Anter NA, El-Sheshtawy HS. Synthesis and evaluation of new polysubstituted quinazoline derivatives as potential antimicrobial agents. Der Pharma Chemica 2012; 4: 1361–1370.*
31. *El-Helby AG, Wahab MH. Design and synthesis of some new derivatives of 3H-quinazolin-4-one with promising anticonvulsant activity. Acta Pharmaceutica 2003; 53(2) :127-138.*
32. *Fajardo A, Linares JF, Martínez JL. Towards an ecological approach to antibiotics and antibiotic resistance genes. Clin Microbiol Infect 2009;15(1) :14-16.*
33. *Faraj FL, Zahedifard M, Paydar M, Looi CY, Majid NA, Ali HM, et al. Synthesis, characterization, and anticancer activity of new quinazoline derivatives against MCF-7 cells. Science World Journal 2014; 14: 1-15.*
34. *Fernandes P, Martens E. Antibiotics in late clinical development. Biochemistry and Pharmacology 2017;133(1):152-63.*
35. *Fleeman R, Horn KSV, Barber MM, Burda WN, Flanigan DL, Manetsch R,Shawa LN. Characterizing the antimicrobial activity of N2,N4-disubstituted quinazoline-2,4- diamines toward multidrug-resistant Acinetobacter baumannii, Antimicrobial Agents and Chemotherapeutics 2017; 61: e00059-17.*
36. *Gatadi S, Gour J, Kaul G, Shukla M, Dasgupta A, Akunuri R, Tripathi R,Madhavi YV, Chopra S, Nanduri S. Synthesis of new 3-phenylquinazolin- 4(3H)-one derivatives as potent antibacterial agents effective against methicillin- and vancomycin-resistant Staphylococcus aureus (MRSA and VRSA) Bioorganic Chemistry 2018;81:175-183*
37. *Gatadi S, Gour J, Shukla M, Kaul G, Das S, Dasgupta A, Madhavi YV,Chopra S, Nanduri S. Synthesis and evaluation of new 4-oxoquinazolin-3(4H)-yl)benzoic acid and benzamide derivatives as potent antibacterial agents effective against multidrug resistant Staphylococcus aureus. Bioorganic Chemistry 2018; 83: 569-579.*
38. *Gatadi S, Lakshmi TV, Nanduri S. 4(3H)-Quinazolinone derivatives: Promising antibacterial drug leads. European Journal of Medicinal Chemistry 2019; 170: 157-172.*
39. *Gatadi, S, Gour J, Shukla M, Kaul G, Das S, Dasgupta A, Malasala S,Borra RS, Madhavi YV, Chopra S, Nanduri S. Synthesis of 1,2,3-triazole linked 4(3H)-Quinazolinones as potent antibacterial agents against multidrug-resistant Staphylococcus aureus. European Journal of Medicinal Chemistry 2018; 157: 1056-1067.*
40. *Georgey H, Abdel-Gawad H, Abbas S. Synthesis and anticonvulsant activity of some squinazolin-4-(3H)-one derivatives. Molecules 2008; 13: 2557-2569.*
41. *Ghorab MM, Gawad SMA, El-Gaby MS. Synthesis and evaluation of some new fluorinated hydroquinazoline derivatives as antifungal agents. Farmacol 2000; 55: 249-255.*
42. *Giri RS, Thaker HM, Giordano T, Chen B, Vasu KK. Synthesis and evaluation of quinazolinone derivatives as inhibitors of NF-kappaB, AP-1 mediated transcription and eIF-4E mediated translational activation: inhibitors of multi-pathways involve in cancer. European Journal of Medicinal Chemistry 2010; 45: 3558-3563.*
43. *Gobinath M, Subramanian N, Alagarsamy V. Design, synthesis and H1-antihistaminic activity of novel 1-substituted-4-(3-chlorophenyl)-[1,2,4] triazo [4,3-a] quinazolin-5(4H)-ones. Journal of Saudi Chemical Society 2015;19:282-6.*
44. *Gulick RM. New antiretroviral drugs. Clinical Microbiology 2003;9(3):186-93.*
45. *H. Ighachane, M.H. Sedra, H. Lazrek, Synthesis and evaluation of antifungal activities of (3H)-quinazolin-4-one derivatives against tree plant fungi,Journal of Material and Environment Sciences 2017; 8: 134-143.*
46. *Hassanzadeh F, Rahmani Khajouei M, Hakimelahi GH, Jafari E, Khodarahmi GA. Synthesis of some new 2,3-disubstituted-4(3H)quinazolinone derivatives. Research in Pharmaceutical Sciences 2012;7:23–30.*
47. *Hemalatha K, Girija K. Synthesis, characterization, preliminaryQSAR studies and in-vitro antioxidant activity of some novel 2,3-disubstituted quinazolinone derivatives. International Journal of Pharmaceutical Sciences 2012; 4: 99–103.*
48. *Hrast M, Jukic M, Patin D, Gobec S, Sova M. Synthesis and structure activity relationship study of novel quinazolinone based inhibitors of Mur A. Bioorganic and Medicinal Chemistry Letter 2017; 27: 3529-3533.*

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 3| March 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

49. *Jadhavar PS, Dhameliya TM, Vaja MD, Kumar D, Sridevi JP,Yogeeswari P, Sriram D, Chakraborti AK. Synthesis, biological evaluation and structure-activity relationship of 2-styrylquinazolones as anti-tubercular agents. Bioorganic and Medicinal Chemistry Letter 2016; 26: 2663-2669.*
50. *Jafari E, Khajouei MR, Hassanzadeh F, Hakimelahi GH, Khodarahmi GA. Quinazolinone and quinazoline derivatives: Recent structures with potent antimicrobial and cytotoxic activities. Research in Pharmaceutical Sciences 2016; 11:1-14.*
51. *Jain N, Jaiswal J, Pathak A, Singour PK. Synthesis, Molecular Docking and Evaluation of 3-{4-[2-amino-4-(substitutedphenyl)-2H-[1,3]oxazin/thiazin-6-yl}2-phenyl-3H quinazolin-4-one Derivatives for their anticonvulsant Activity. Medicinal Chemistry 2018;18(1):63-73.*
52. *Jain N, Jaiswal J, Pathak A, Singour PK. Synthesis, Molecular docking and evaluation of 3-{4-[2-amino-4-(substitutedphenyl)-2H-[1,3]oxazin/thiazin-6-yl}-2-phenyl-3H-quinazolin-4-one derivatives for their anticonvulsant activity. Central Nervous System agents Medicinal Chemistry 2018; 18: 63-73.*