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SYNTHESIS, STRUCTURAL CHARACTERIZATION AND BIOLOGICAL EVALUATION OF A NEW SERIES OF QUINAZOLINONE INTEGRATED NOVEL PYRAZOLE VIA CHALCONE

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ABSTRACT

In the present investigation a new class of Pyrazole derivatives containing Quinoline moiety has been designed and synthesized by refluxation of 6,8-dibromo-3-{4-[3-(substitutedphenyl) prop-2-enoyl]phenyl}-2-phenylquinazolin-4-one (0.01M) and 99% hydrazine hydrate (0.015M) by using ethanol (50ml) as a solvent. The intermediate 6, 8-dibromo-3-{4-[3-(substitutedphenyl) prop-2-enoyl] phenyl}-2-phenylquinazolin-4-one synthesized by condensation of 3-(4-acetylphenyl)-6,8-dibromo-2-phenylquinazolin-4-one with various aldehydes in presence of ethanol. The product is characterized by spectral and analytical data. The chemical structures of the products are confirmed by IR, NMR and spectral data.

KEYWORDS: Pyrazole, Chalcone, Antimicrobial activity, Antifungal activity, Agar cup method.

INTODUCTION

The chemistry of heterocyclic compounds is one of the most complex and important streams of organic chemistry. It plays an important role in regulating biological process. Much attention has paid to the synthesis of heterocyclic compounds bearing nitrogen containing ring system, like pyrazoline mainly due to their higher pharmacological activity. Literature studies have shown that pyrazoline and their derivatives possess versatile type of biological activities such as anticancer,[1] Selective COX-2 Inhibitors,[2] cytotoxic,[3] antifungal,[4] antitubercular,[5] anti-AIDS,[6] anti-inflammatory activity, antioxidant[7] Some pyrazole scaffold has application in Alzheimer's disease and Parkinson's disease treatment.[8]

Looking at the importance of pyrazole nucleus, it was thought that it would be worthwhile to design and synthesize some new quinoline derivatives bearing pyrazole moiety and evaluate them for potential biological activities. So, it was planned to synthesize some new substituted pyrazoles from chalcones with the hope that they may possess better antimicrobial activities.

EXPERIMENTAL

1. Materials and Methods

All reagents were purchased from commercial suppliers and all reagents of analytical reagent grade and were used without further purification, All the product were synthesized and characterized by their spectral analysis.

Melting points were taken in open capillary tube. The IR spectra were recorded on Bruker Model; Alpha, Laser Class1, made in Germany and Brooker instrument used for NMR Spectroscopy was 500 MHz. Tetramethyl silane was used as an internal standard and DMSO was used as a solvent. Purity of the compounds was checked by TLC on silica-G plates. Antimicrobial activities were tested by Agar Cup method. Standard drugs like Streptomycin and Fluconazole were used for the comparison purpose.

2. General Procedure and Detection Method

Preparation of 3-(4-acetylphenyl)-6, 8-dibromo-2-phenylquinazolin-4-one (KS-1).

In a conical flask, a mixture of 6, 8-dibromo-2-phenyl-3,1-benzoxazin-4-one (3.8gm,0.01 mole) and 1-(4-aminophenyl) ethanone (1.35gm, 0.01mole) was heated together upon fusion at 150^0C on sand bath for 2 hours. After cooling, the crude mass was crystallized twice from ethanol. The yield of the product was 75% and the product melts at 240^0 C.

IR (KBr); KS-01 (cm^{-1}): 3063 (=C-H), 2982 (-C-H Stretching), 1683 (>C=O Stretching), 1584 (>C=N stretching), 1560 (>C=C< Aromatic), 1429 (-CH_3), 1311 (C-N), 568 (C-Br).

^{1}HNMR (DMSO); (KS-01): δ ppm 2.543, Singlet (3H) (-$COCH_3$), 7.260-8.277, Multiplet (11H)(Ar-H).

Preparation of 6, 8-dibromo-3-{4-[3-(substitutedphenyl)prop-2-enoyl]phenyl}-2-phenylquinazolin-4-one (KS-2a-2j).

To the solution of 3-(4-acetylphenyl)-6,8-dibromo-2-phenylquinazolin-4-one (0.01M) in absolute ethanol (50 ml), substituted benzaldehyde (0.01M) and 2% NaOH (10 ml) were added and refluxed for 10 hours. After refluxing the reaction mixture was concentrated, cooled, filtered and neutralized with dil. HCl. The solid residue thus obtained was crystallized by absolute ethanol.

IR (KBr); 2e (cm^{-1}): 6, 8-dibromo-3-{4-[3-(2-hydroxyphenyl)prop-2-enoyl]phenyl}-2-phenylquinazolin-4-one. 3230 (-OH), 3065 (=C-H), 1679 (>C=O Stretching), 1584 (>C=N stretching), 1552 (>C=C< Aromatic), 1317 (C-N), 536 (C-Br).

IR (KBr); 2h (cm^{-1}): 6, 8-dibromo-3-{4-[3-(4-dimethylaminophenyl)prop-2-enoyl]phenyl}-2-phenylquinazolin-4-one. 3051 (=C-H), 2965 (-C-H Stretching), 1679 (>C=O Stretching), 1585 (>C=N stretching), 1515 (>C=C< Aromatic), 1445 (-CH_3), 1312 (C-N), 546 (C-Br)

^{1}HNMR (DMSO); 2h: 6, 8-dibromo-3-{4-[3-(4-dimethylaminophenyl) prop-2-enoyl]phenyl}-2-phenylquinazolin-4-one. δ ppm, 2.827, Singlet (6H) (-$N(CH_3)_2$) 7.942, Doublet (2H) (-CH=CH-), 7.170 - 8.247, Multiplet (15H) (Ar-H).

^{1}HNMR (DMSO); 2i: 6, 8-dibromo-3-{4-[3-(4-methoxyphenyl)prop-2-enoyl]phenyl}-2-phenylquinazolin-4-one. δ ppm, 3.867 , Singlet (3H) (-OCH_3), 7.858 , Doublet (2H) (-CH=CH-), 7.009 - 8.251 , Multiplet (15H) (Ar-H)

Preparation of 6, 8-dibromo-3-{4-[5-(substitutedphenyl)-4, 5-dihydro-pyrazol-3-yl]phenyl}-2-phenylquinazolin-4-one (KS-3a-3j)

A mixture of 6, 8-dibromo-3-{4-[3-(substitutedphenyl)prop-2-enoyl]phenyl}-2-phenylquinazolin-4-one (0.01M) and 99% hydrazine hydrate (0.015M) in ethanol (50ml) refluxed gently for 3 hours. Then the mixture was concentrated and allowed to cool. The resulting solid was filtered, washed with ethanol and recrystallized from ethanol.

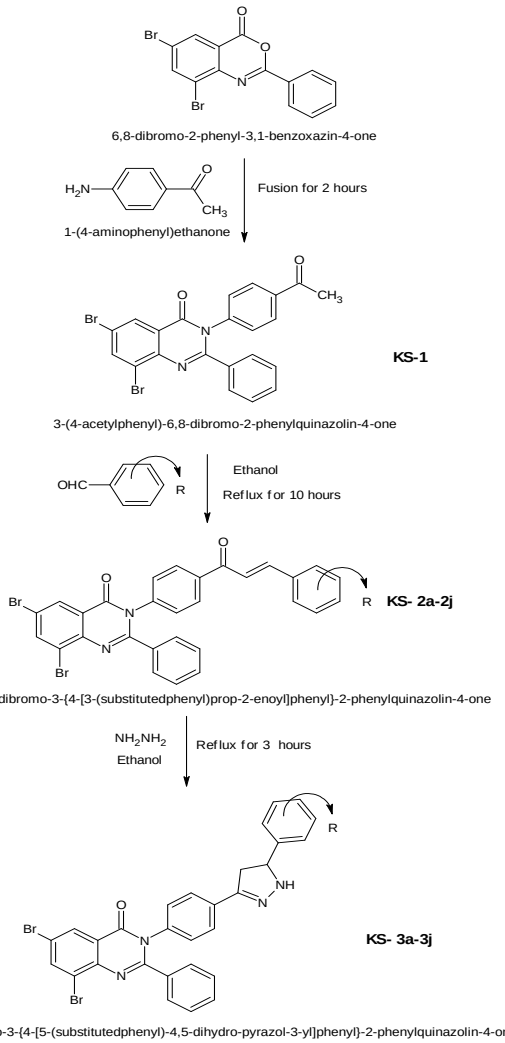
IR (KBr); 3c (cm^{-1}): 6, 8-dibromo-3-{4-[5-(3, 4-dimethoxyphenyl)-4, 5-dihydro-pyrazol-3-yl]phenyl}-2-phenylquinazolin-4-one. 3313 (>NH-), 3096 (=C-H), 2916 (-C-H Stretching), 1664 (>C=O Stretching), 1566 (>C=N stretching), 1511 (>C=C< Aromatic), 1446 (-CH_2 bending), 1356 (-CH_3), 1313 (C-N), 1259 (N-N), 1235 (C-O-C), 532 (C-Br).

IR (KBr); 3j (cm^{-1}): 6, 8-dibromo-3-{4-[5-(3-nitrophenyl)-4,5-dihydro-pyrazol-3-yl]phenyl}-2-phenylquinazolin-4-one. 3345 (>NH-), 3098 (=C-H), 2928 (-C-H Stretching), 1678 (>C=O Stretching), 1581 (>C=N stretching), 1538 (>C=C< Aromatic), 1448 (-CH_2 bending), 1313 (C-N), 1250 (N-N), 1555 (N=O), 555 (C-Br).

^{1}HNMR (DMSO); (KS-3e): 6, 8-dibromo-3-{4-[5-(2-hydroxyphenyl)-4, 5-dihydro-pyrazol-3-yl]phenyl}-2-phenylquinazolin-4-one. δ ppm, 3.365, Doublet (2H) (-CH_2), 3.966, Triplet (1H) (-CH<), 6.975 – 7.708, Multiplet (15H) (Ar-H), 7.385, Singlet (1H) (-NH), 9.012, Singlet (1H) (-OH).

^{1}HNMR (DMSO); (KS-3j): 6, 8-dibromo-3-{4-[5-(3-nitrophenyl)-4,5-dihydro-pyrazol-3-yl]phenyl}-2-phenylquinazolin-4-one. δ ppm, 3.367, Doublet (2H) (-CH_2), 3.958, Triplet (1H) (-CH<), 7.258 -7.962, Multiplet (15H) (Ar-H), 7.406, Singlet (1H) (-NH).

Reaction Scheme



RESULT AND DISCUSSION

Table no. 1: Physical constant of 6, 8-dibromo-3-{4-[5-(substitutedphenyl)-4,5-dihydro-pyrazol-3-yl]phenyl}-2-phenylquinazolin-4-one

Sr. no	Comp.	R	M.F.	Mol.Wt (g/mole)	Yield %	M.P °C	% Carbon		%Nitrogen		% Hydrogen	
							Found	Calcd	Found	Calcd	Found	Calcd
1	KS-3a	-2-Cl	$C_{29}H_{19}Br_2ClN_4O$	634.74	62	183	54.83	54.87	8.82	8.83	3.02	3.02
2	KS-3b	-4-Cl	$C_{29}H_{19}Br_2ClN_4O$	634.74	75	147	54.84	54.87	8.80	8.83	3.02	3.02
3	KS-3c	-3,4-$(OCH_3)_2$	$C_{31}H_{24}Br_2N_4O_3$	660.35	82	170	56.35	56.38	8.47	8.48	3.65	3.66
4	KS-3d	-H	$C_{29}H_{20}Br_2N_4O$	600.30	73	163	58.02	58.02	9.31	9.33	3.33	3.36
5	KS-3e	-2-OH	$C_{29}H_{20}Br_2N_4O_2$	616.30	68	160	56.50	56.52	9.04	9.09	3.23	3.27
6	KS-3f	-4-OH-3-OCH_3	$C_{30}H_{22}Br_2N_4O_3$	646.32	70	156	55.74	55.75	8.62	8.67	3.40	3.43
7	KS-3g	-4-OH	$C_{29}H_{20}Br_2N_4O_2$	616.30	87	190	56.50	56.52	9.09	9.09	3.25	3.27
8	KS-3h	-4-$N(CH_3)_2$	$C_{31}H_{25}Br_2N_5O$	643.37	83	120	57.86	57.87	10.88	10.89	3.92	3.92
9	KS-3i	-4-OCH_3	$C_{30}H_{22}Br_2N_4O_2$	630.32	72	138	57.16	57.16	8.87	8.89	3.52	3.52
10	KS-3j	-3-NO_2	$C_{29}H_{19}Br_2N_5O_3$	645.30	78	206	53.95	53.98	10.82	10.85	2.96	2.97

Structures of KS-3a to KS-3j

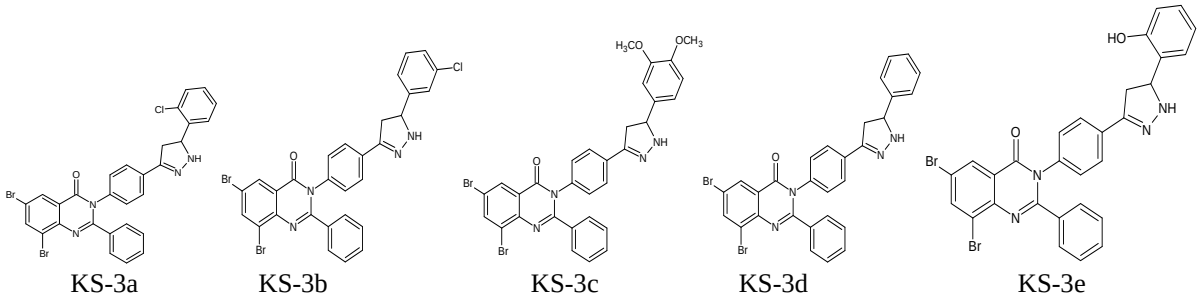
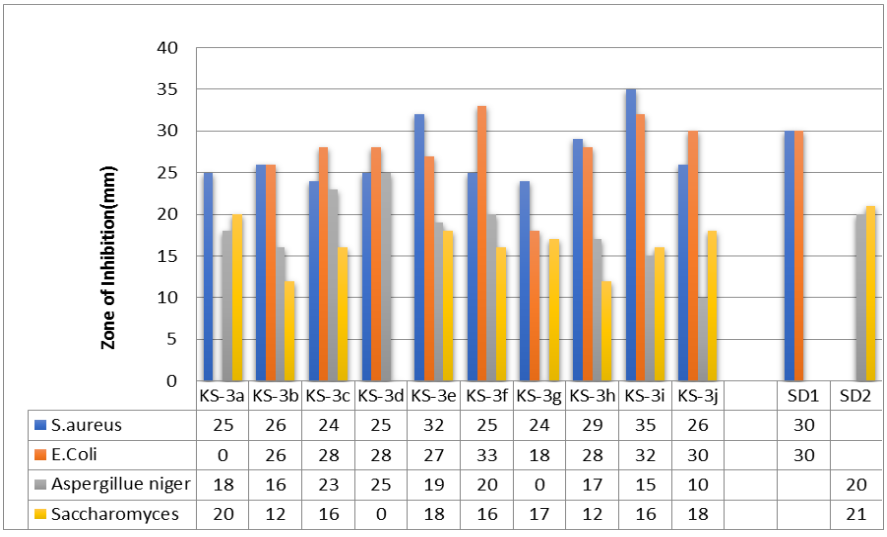


Table No. 2 (3a to 3j): Antimicrobial activity of 6,8-dibromo-3-{4-[5-(substitutedphenyl)-4,5-dihydro-pyrazol-3-yl]phenyl}-2-phenylquinazolin-4-one



	KS-3a	KS-3b	KS-3c	KS-3d	KS-3e	KS-3f	KS-3g	KS-3h	KS-3i	KS-3j		SD1	SD2
S.aureus	25	26	24	25	32	25	24	29	35	26		30	
E.Coli	0	26	28	28	27	33	18	28	32	30		30	
Aspergillue niger	18	16	23	25	19	20	0	17	15	10			20
Saccharomyces	20	12	16	0	18	16	17	12	16	18			21

Table no. 3: Antimicrobial activity of 6, 8-dibromo-3-{4-[5-(substitutedphenyl)-4,5-dihydro-pyrazol-3-yl]phenyl}-2-phenylquinazolin-4-one.

Sr. no.	Comp no.	R	Zone of inhibition in mm			
			Antibactrerial activity		Antifungal activity	
			S. Aureus	E. Coli	Aspergillus niger	Saccharomyces
1	Ks-3a	2-cl	25	Na	18	20
2	Ks-3b	4-cl	26	26	16	22
3	Ks-3c	-3,4-$(och_3)_2$	24	28	18	16
4	Ks-3d	-h	25	28	25	Na
5	Ks-3e	-2-oh	32	27	19	18
6	Ks-3f	-4-oh-3-och_3	25	33	20	16
7	Ks-3g	-4-oh	24	18	Na	17
8	Ks-3h	-4-n$(ch_3)_2$	29	28	17	12
9	Ks-3i	-4-och_3	35	32	15	16
10	Ks-3j	-3-no_2	26	30	10	18

Antibacterial activity

From screening results, compound 3i, 3e were found to possess maximum antibacterial activity against Staphylococcus aureus and 3f, 3i against Escherichia Coli which showed good anti-bacterial activity than the respective standard test-drug also**.** Minimum antibacterial activity was shown by the compounds 3c against S. aureus and 3g against E. coli. KS-3a was found to be inactive against E. coli. Rests of all compounds were found to show moderate to excellence antibacterial activity against S. aureus and E. coli.

Antifungal activity

Biological evaluation of present investigation revealed maximum antifungal activity was shown by the compound 3d and 3b against Aspergillus niger and Saccharomyces respectively. The minimum antifungal activity was shown by the compound KS-3j and 3h against Aspergillus niger and Saccharomyces respectively. 4e was found to be inactive against Aspergillus niger. Remaining other synthesized compounds were found to show good to moderate antifungal activity against Aspergillus Niger and Saccharomyces.

CONCLUSION

The Main objective of present research work was to synthesize, characterize and evaluate antimicrobial activities of the newly synthesized compounds with the help of analytical data such as IR and ^{1}H-NMR. In conclusion, in present we prepared a series of 6,8-dibromo-3-{4-[5-(substitutedphenyl)-4,5-dihydro-pyrazol-3-yl]phenyl}-2-phenylquinazolin-4-one.. Over all evaluation of the synthesized (3a-3j) compounds suggests that most of them were found to show moderate to excellence antibacterial and antifungal activity as compared to the standard drugs like Streptomycin and Fluconazole respectively.

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REFERENCES

1. Usama Fathy, Ameen A. Abu-Hashem, Rasha S. Gouhar, Hanem M. Awad and Abdelbaset M. Elgamal, synthesis, structural characterization of some pyrazolo [1-5a] pyrimidine and imidazo[1,2-b]- pyrazole derivatives as anti-cancer activity, *Rasayana Journal of Chemistry*, 2021; 14(2): 741-750. DOI: 10.31788/ RJC.2021.1426137
2. Mohyeddin Assali , Murad Abualhasan , Hadeel Sawaftah, Mohammed Hawash , and Ahmed Mousa, Synthesis, Biological Activity, and Molecular Modeling Studies of Pyrazole and Triazole Derivatives as Selective COX-2 Inhibitors, *Hindawi Journal of Chemistry*, 2020; 2020: 1-14. DOI: 10.1155/2020/6393428
3. Esvet Akbas1, Fatih Caglar Celikezen, Hasan Turkez, Ozlem Ozdemir3, Adem Ruzgar, Erdem Ergan and Ertan Sahin Akbas, Synthesis of the 3,5-diphenyl-1*H*-pyrazole and cytogenetic and oxidative alterations after exposure of cultured human whole blood cells, *Cogent Chemistry*, 2017; 3: 1-10. DOI: 10.1080/23312009.2017.1344115
4. J. J. Liu, M. Y. Zhao, X. Zhang, X. Zhao, H. L. Zhu, Pyrazole Derivatives as Antitumor, Anti-Inflammatory and Antibacterial agents, *Mini-Reviews in Medicinal Chemistry*, 1957; 13: 2013. DOI: 10.2174/13895575113139990078
5. V. Alagarsamy, V. R. Solomon, G. Krishnamoorthy, M. T Sulthana, B. Narendar, ***Journal of the Serbian*** *Chemical Society***,** 2015; 80(12): 1471-1479. DOI: 10.2298/JSC150103053A
6. Sony JK, Ganguly S. A battle against AIDS: New pyrazole key to an older lock-reverse transcriptase, *International Journal of Pharmacy and Pharmaceutical Sciences*, 2016; 8: 75-79. DOI:10.22159/ijpps.2016v8i11.12634
7. Vishwanath Sharath, Honnaiah Vijay Kumar, Nagaraja Naik, Synthesis of novel indole-based scaffolds holding pyrazole ring as anti-inflammatory

and antioxidant agents, *Journal of Pharmacy Research*, 2013; 6: 785-790 DOI: 10.1016/j.jopr.2013.07.002

8. Xuefei Li, Yanbo Yu and Zhude Tu, Pyrazole Scaffold Synthesis, Functionalization, and Applications in Alzheimer's Disease and Parkinson's Disease Treatment (2011–2020), *Molecules*, 2021; 26: 1-38, DOI: 10.3390/molecules26051202