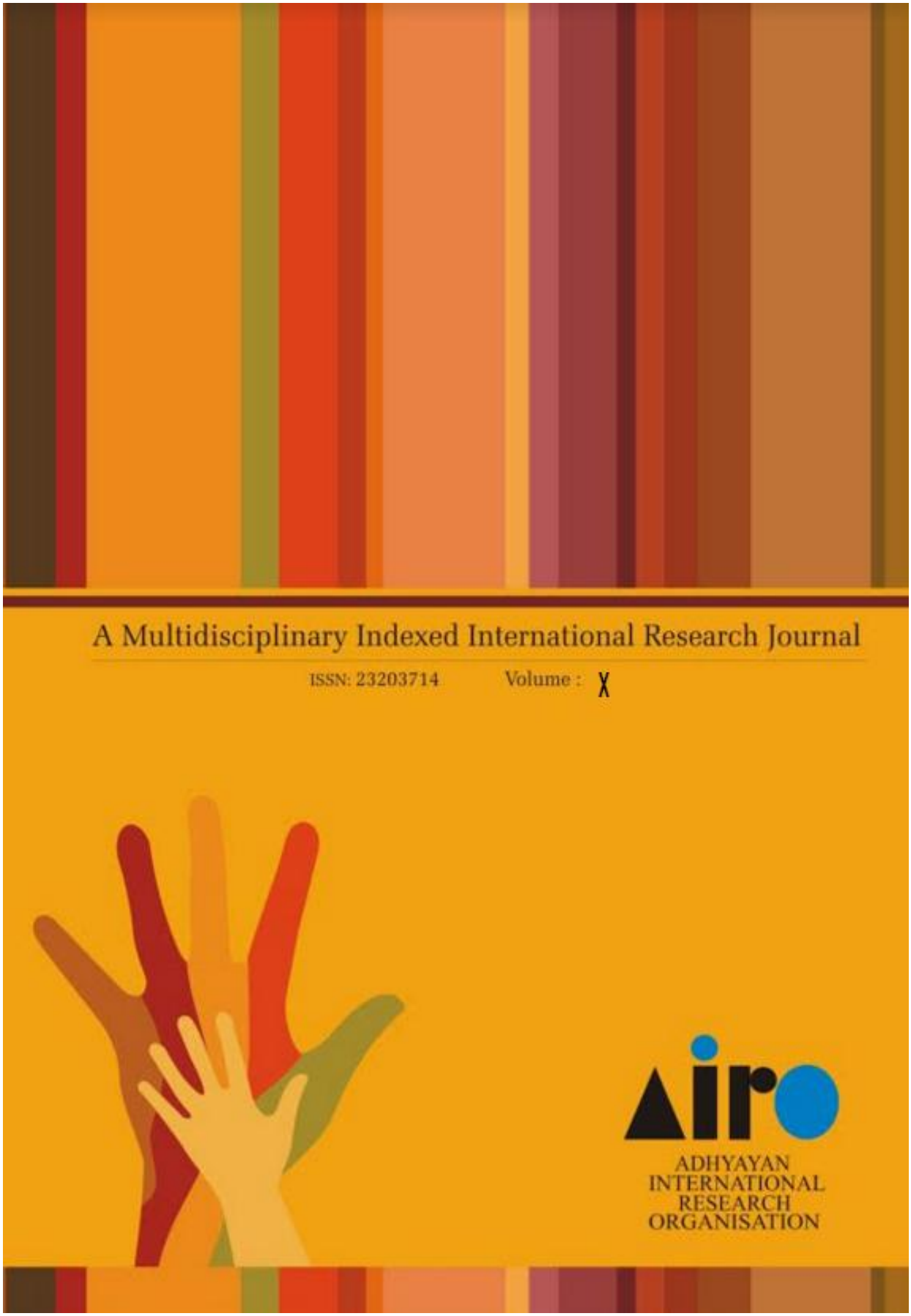
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A novel approach for the biological evaluation of iodoquinazoline along with their synthesis and characterization

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ABSTRACT

A novel arrangement of 6-Iodoquinazolin-4-one subordinates were orchestrated and assessed for their antibacterial and antifungal exercises against gram negative viz Escherichia coli, P.aeruginosa and gram positive microorganisms viz staphylococcus aures, Bacillus subtilis and Bacillus cereus and pathogenic organisms viz Candida albicans and Saccharomyces cerevisiae. Streptomycin and Nystatin utilized as standard drugs. Every one of the compounds were described by physical and unearthly information. Every one of the compounds demonstrated strong to respectably powerful antimicrobial action. These compounds can be additionally misused to get the powerful lead compound. The point by point synthesis and the antimicrobial screening of the new compounds are accounted for. With comparable procedures, recorded execution information of the gadget can give a specific level of confirmation. Be that as it may, with new items and new procedures, there is the requirement for a superior comprehension of the personality of the buildup, as well as of the hugeness of the deposit. [1].

Keywords: Quinazolinone, Benzimidazole, Antibacterial activity, Antifungal activity.

INTRODUCTION

Heterocyclic science is a science including the heterocyclic compounds which contain iotas of no less than two distinct components as number of ring. The heterocyclic might be inorganic, however the compound has carbon molecules in the ring, the word hetero implies not quite the same as carbon and hydrogen. Nitrogen containing heterocyclic compounds assumes an imperative part in therapeutic science. Quinazolinone comprises of two combined benzene and pyrimidinone ring. Quinazolinones are a substantial class of dynamic concoction compounds displaying a wide range of organic exercises in creatures and in addition in humans. Writing thinks about on quinazolinones have demonstrated that these subordinates have a

wide assortment of natural exercises, for example, cancer prevention agent, antifungal, antibacterial, anticonvulsant[2], against inflammatory[3], antihyperlipidemic[4], anticancer[5], antimalarial[6], antispasmodial[7], analgesic[8], antiviral[9], antitubercular[10] and antimicrobial[11] exercises.

As of late much consideration has been centered around the synthesis of some Quinazolinone compounds as potential antimicrobial operators. In the present examination, the quinazoline analogs were intended to contain a legitimate side chain bearing sulfur gather which are accepted to add to the antimicrobial movement, what's more, some heterocyclic rings that referred to have antimicrobial action, for example, benzimidazole has been joined into the quinazolinone core. The recently combined compounds were screened for their movement against a board of Gram-positive and Gram-negative microscopic organisms and pathogenic growths [12].

EXPERIMENTAL AREA

The liquefying purpose of the compounds was resolved in open slender tube and values are uncorrected. Microanalyses were led on a Heraeus instrument; results are inside ± 0.4% of the hypothetical qualities. TLC was completed on a precoated plate (silica gel 60F-254, Merck) and spots were envisioned with Iodine (or) UV light. IR spectra were recorded in KBr plates on a Brooker FTIR Spectrophotometer. The virtue of the recently blended compounds was prove by HPLC (Agilent) and their natural examination was for the most part observed to be in concurrence with the structure. 1H-NMR spectra were recorded on a JOEL-JNM EX-90 FT-NMR, (90 MHZ) Spectrometer in CDCl3/DMSO-d6 as a dissolvable, the synthetic shifts(δ) are communicated in ppm utilizing TMS as inner standard. Every one of the solvents utilized were of expository review [13].

3-(4-Chlorophenyl)-6-iodo-2-mercaptoquinazolin-4(3H)-thione (IQZN-3):

To an answer of IQZN (3-(4-Chlorophenyl)-6-iodo-2-mercaptoquinazolin-4(3H)- one) (4.145 g in 0.01 mol) in dry xylene (40 ml) phosphorous pentasulfide (2.3 g, 0.01 mol) was included. The response blend was refluxed for 18 hr, cooled and dissolvable was vanished under vacuo. The got strong was treated with acidulated icy water (100 ml) with mixing for 15 min (Fig 1). The acquired strong was separated, washed with water, dried and solidified from ethanol (Table 1, 2). 1H NMR (DMSO-d_6): δ 7.38 (d, 1H, J = 7.5 Hz, Quin-H), 7.52 (d, 2H, J = 8.5 Hz, Ar-H), 7.66 (d, 2H, J = 8.5 Hz, Ar-H), 8.06-8.19 (dd, 1H, J = 2, 7.5 Hz, Quin-H), 8.29 (d, 1H, J = 2 Hz, Quin-H), 12.3 (brs, ^{1}H, NH).

3-(4-Chlorophenyl)-6-iodo-2[N-4-bromophenyl) carbamoylthio]-4-(3H)-quinzolin-4-one (IQZN-4):

To an answer of IQZN (3-(4-Chlorophenyl)-6-iodo-2-mercaptoquinazolin-4(3H)- one) (4.14 g, 0.01 mol) in CH3)2CO (60 ml), anhydrous K2CO3 (2.0 g) was included, trailed by the fitting N-(4-bromophenyl)- 2-chloroacetamide (0.012 mol). The response blend was warmed under reflux for 20 h, then separated while hot and the filtrate was amassed in vacuo (Fig 1). The isolated strong was sifted, washed with water, dried and solidified from the reasonable dissolvable (Table 1). ^{1}H NMR (DMSO-d_6): 4.28 (s, 2H, S-CH_2CO), 7.08-7.81 (m, 9H, Ar-H and Quin-H), 3.03-8.19 (dd, 1H, J = 2, 7.5 Hz, Quin-H), 8.31 (d, 1H, J = 2 Hz, Quin-H), 11.86 (brs, 1H, NH).

2-(2-Benzimidazolylmethylthio)-3-(4-chlorophenyl)-6-iodo-(3*H*)-quinazolin-4-one (IQZN-5):

To an answer of IQZN (3-(4-Chlorophenyl)-6-iodo-2-mercaptoquinazolin-4(3H)- one) (2.07 g, 0.005 mol) in CH3)2CO (40 ml), anhydrous potassium carbonate (2.0 g) was included, trailed by 2-chloromethylbenzimidazole (1 g, 0.0065 mol). The response blend was warmed under reflux for 20 h (Fig 1). The dissolvable was expelled in vacuo and the got strong was solidified from ethanol (Table 1, 2). ^{1}H NMR (DMSO-d_6), δ 3.91 (s, 2H, S-CH2-Hetero), 7.26-7.72 (m, 10H, Ar-H, benzimidazole-H, NH and Quin-H), 8.05-8.19 (dd, 1H, J = 2, 7.5 Hz, Quin-H), 8.29 (d, 1H, J =2Hz, Quin-H).

2-Amino-3-(4-chlorophenyl)-6-iodoquinazolin-4(3H)-one (IQZN-1):

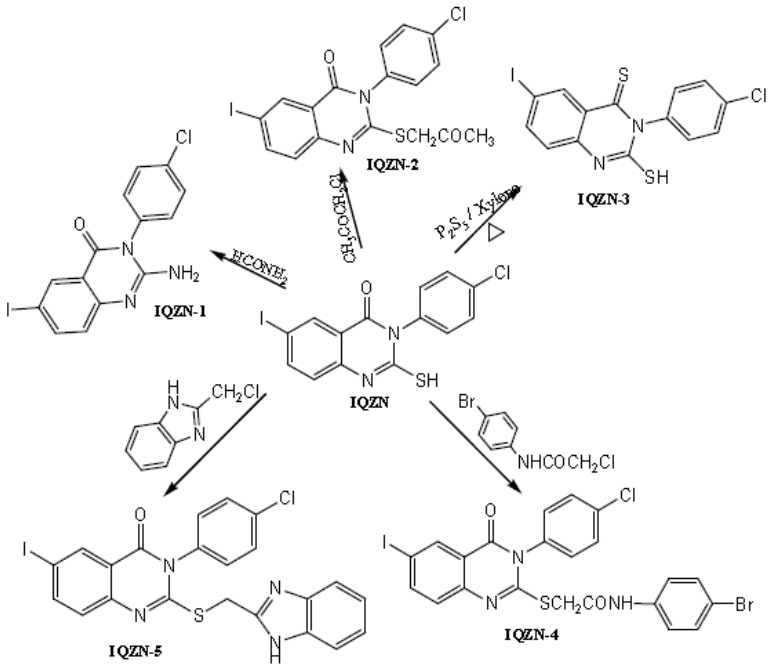
An answer of IQZN (3-(4-Chlorophenyl)- 6-iodo-2-mercaptoquinazolin-4(3H)- one) (2.07 g, 0.005 mol) in formamide (20 ml) was warmed under reflux for 20 h. On cooling, the acquired encourage was separated (Fig 1), washed with water and solidified from ethanol (Table 1, 2). ^{1}H NMR (DMSO-d_6): δ 5.92 (brs, 2H, NH2), 7.41 (d, 1H, J = 7.5 Hz, Quin-11), 7.52 (d, 2H, J = 8.5 Hz, Ar-H), 7.67 (d, 2H, J = 8.5 Hz, Ar-H), 8.04-8.19 (dd, 1H, J = 2, 7.5 Hz, Quin-11), 8.31 (d, 1H, J = 2 Hz, Quin-H).

2-(2-Oxopropylthio)-3-(4-chlorophenyl)-6-iodoquinazolin-4(3H)-one (IQZN-2):

To an answer of IQZN (3-(4-Chlorophenyl)-6-iodo-2-mercaptoquinazolin-4(3H)- one) (4.15 g, 0.01 mol) in dry CH3)2CO (50 ml), anhydrous potassium carbonate (2.0 g) was included, trailed by chloroacetone (0.015 mol)[14]. The response blend was warmed under reflux for 20 h, sifted while hot and the filtrate was gathered in vacuo (Fig 1). The isolated unrefined item was separated, dried and solidified from ethanol (Table 1, 2). ^{1}H NMR ($CDCl_3$): δ 2.15 (s, 3H, CH_3CO), 4.32 (s, 2H, CH_2CO), 7.41 (d, 1H,

J = 7.5 Hz, Quin-H), 7.53 (d, 2H, J = 8.5 Hz, Ar-H), 7.68 (d, 2H, J = 8.5 Hz, Ar-H), 8.02-8.18 (dd, 1H, J = 2, 7.5 Hz, Quin-H), 8.31 (d, 1H, J = 2 Hz, Quin-H).

Figure 1: Synthesis of Iodoquinazolinone derivatives Synthesis of Iodoquinazolinone derivatives



RESULTS AND DISCUSSION

Chemistry:

The manufactured methodology to get the objective compounds IQZN-1 – IQZN-5 is portrayed in Schemes 1. The beginning material IQZN (3-(4-Chlorophenyl)- 6-iodo-2-mercaptoquinazolin-4(3H)- one) was treated with formamide to get 2-Amino-3-(4-chlorophenyl)- 6-iodoquinazolin-4(3H)-one (IQZN-1). Alkylation of IQZN (3-(4-Chlorophenyl)- 6-iodo-2-mercaptoquinazolin-4(3H)- one) with chloroacetone gave the 2-oxopropylthio simple 2-(2-Oxopropylthio)- 3-(4-chlorophenyl)- 6-iodoquinazolin-4(3H)- one (IQZN-2). 3-(4-Chlorophenyl)- 6-iodo-2-mercaptoquinazolin-4(3H)- one was treated with phosphorous pentasulphide in bubbling xylene to bear the cost of the 4-thioxo subsidiary 3-mercaptoquinazoline-4(3H)-thione (IQZN-3) in high return. Treatment of IQZN (3-(4-Chlorophenyl)- 6-iodo-2-mercaptoquinazolin-4(3H)- one) with N-(4-bromophenyl)- 2-chloroacetamide (0.012 mol) managed 3-(4-Chlorophenyl)- 6-iodo-2[N-4-bromophenyl) carbamoylthio]-4-(3H)- quinzoline-4-one (IQZN-4). Treatment of IQZN (3-(4-Chlorophenyl)- 6-iodo-2-mercaptoquinazolin-4(3H)- one) with 2-chloromethyl benzimidazole managed 2-(2-Benzimidazolylmethylthio)- 3-(4-

chlorophenyl)- 6-iodo-(3H)- quinazoline-4- one **(IQZN-5)**.

Table 1: The physiochemical properties of the synthesized compounds

Compd	Solvent	M.P.^{0}C	Yield	Molecular formula
IQZN-1	Ethanol	240-242	41	$C_{14}H_9ClIN_3O$
IQZN-2	Ethanol	195-197	68	$C_{17}H_{12}ClIN_2O_2S$
IQZN-3	Ethanol	290-292	70	$C_{14}H_8ClIN_2S_2$
IQZN-4	Ethanol, dioxane	245-247	66	$C_{22}H_{14}BrClIN_3O_2S$
IQZN-5	Ethanol	260-262	40	$C_{22}H_{14}ClIN_4OS$

Table 2: Mass spectral data of some compounds

Compd	MS (Relative Intensity)
IQZN-1	m/z (M+, 397 91.96), 399 (M + 2, 30.23), 258.3 (38.20), 244 (63.61).
IQZN-3	m/z (M+, 430 32.82), 432 (M + 2, 11.40); 319 (1.81), 287 (37.69), 144 (70.59).
IQZN-4	m/z (M+, 625 0.71), 627 (M + 2, 0.23), 514 (14.31), 455 (6.47), 427 (9.31), 413 (3.61), 381 (2.12).
IQZN	m/z (M+, (1.23), 413 (2.13), 381 (0.8).

-5	544 2.93), 427

Antimicrobial Activity:

All the tried compounds alongside standard [15]streptomycin and nystatin were screened in-vitro for antimicrobial action against gram positive microbes Staphylococcus aureus (ATCC 06538), Bacillus subtilis (RTCC 6633), Escherichia coli (ATCC 10536) and pathogenic growths Candida albicans (ATCC 1023) and Saccharomyces cerevisiae (ATCC 9763)[16].

Supplement agar plates were seeded utilizing 0.1 ml of overnight societies. Tube shaped attachments were expelled from agar plate utilizing a sterile stopper borer and 100 µg of the tried compounds (1 mg/ml, DMSO) were added to the well in triplicates. Clear dissolvable was utilized as control. Plates vaccinated with tried microscopic organisms were brooded at 370C, while those of growths were hatched at 300C. Results were taken after 24 h of hatching and were recorded as normal breadth of the hindrance zone in mm [17].

Table 3: Antimicrobial screening results for the tested compounds at 1 mg/ml concentration

Comp	*E. coli*	*S. aureus*	*B. subtilis*	*S. cerevisiae*	*C. albicans*
IQZN-1	*++*	*++*	*++*	--	--
IQZN-2	*+*	*+*	*+*	--	--
IQZN-3	--	--	*+*	*++*	*++*
IQZN-4	*++*	*++*	--	*+*	--
IQZN-5	*+++*	*+++*	*+++*	*+++*	*+++*
Streptomycin	*+++*	*+++*	*++*	*NT*	*NT*
Nystatin	*NT*	*NT*	*NT*	*++*	*+++*

Inactive (inhibition zone < 10 mm), +, moderately activity (inhibition zone 10-15 mm), ++: active (inhibition zone 15-20 mm), +++: marked activity (inhibition zone > 20 mm), NT: not tested.

CONCLUSION

The greater part of the recently integrated compounds were subjected to antimicrobial screening by the in vitro glass plate procedure utilizing Streptomycin and Nystatin as positive controls. Compound IQZN-5 demonstrated exceptional movement toward the Gram negative microbes E. coli. The Gram positive microscopic organisms S. aureus and B. subtilis ended up being delicate toward compounds IQZN-1 and IQZN-5. Compound IQZN-5 demonstrated astounding action towards the utilized growths S. cerevisiae and C. albicans. The majority of the previously mentioned compounds demonstrated antimicrobial movement practically identical to the utilized positive control drug. Furthermore compounds IQZN-5 turned out to be the most dynamic expansive range antimicrobial specialists in this review.

Taking everything into account, the present review uncovered that connection of benzimidazole to the quinazolinone core could be helpful as a format for further advancement through change or derivatization to plan more strong antimicrobial specialists.

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