RESEARCH PAPER

Synthesis and Tripartite Biological Assessment of Quinazolinone Schiff Base Derivatives: Antimicrobial, Antioxidant, and Anticancer Activities

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ABSTRACT

The aim is to synthesis a new series of 3-substituted quinazolinone derived Schiff base derivatives through the Niementowski reaction, analyse their physico-chemical and pharmacokinetic properties using computational methods, and assess their in vitro biological activities like anti-cancer, antimicrobial and antioxidant activity for the selected newly synthesized lead molecule. The novel 10 synthesized lead compounds were analysed for their physical characters, viz colour, molecular formula, molecular weight, percentage yield and melting point, log p and Rf value. IC50 is the concentration of an inhibitor/sample/ formulation at which the viable cells are reduced by half for anticancer activity by MTT assay, Sample QZT-3b was found to be the most cytotoxic among all the samples against human cancer cell lines HepG2 cell lines. QZT-3b, QZT-4a and QZT-2c showed good MIC values and very effective at the amount 125µg/ml whereas samples QZT-2a and QZT-3a does not seem to impose antimicrobial effect till 1000µmol/disc for antimicrobial activity performed by disc diffusion method. An In vitro antioxidant activities of these quinazolinone derived Schiff base derivatives were evaluated and compared with standard antioxidants ascorbic acid (AA) employing 1,1-diphenyl-2-picryl-hydrazyl (DPPH) assay. The results showed that the IC50 of QZT-3b(3.1 µg/ml), QZT-4a(4.0 µg/ml) and QZT-2c(5.0 µg/ml) were lower than IC50 of standard ascorbic acid(5.5µg) performed in DPPH antioxidant assay indicating very good activities of these compounds and was found equivalent to 5.5µg of standard Ascorbic acid for antioxidant activity.

Keywords: Quinazolinone, Anti-Cancer, Antimicrobial, Antioxidant Activity and Schiff Base.

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INTRODUCTION:

In the world of modern medicine, we are currently facing a double-edged sword. On one side, common infections are becoming harder to treat due to antibiotic resistance; on the other, the complexity of diseases like cancer requires smarter, more versatile treatments. This challenge has pushed us to look for "multi-tasking" molecules—single compounds that can wear multiple hats as antioxidants, germ-fighters, and tumor inhibitors. Therefore, there is an urgent need to continue searching for new medication therapies that are cost-effective, more effective, and less hazardous. Heterocyclic nucleus-containing compounds have garnered significant attention in the field of medicinal chemistry. Many heterocyclic compounds have been synthesized and showed potential anti-cancer activity. These compounds are designed to interact with various targets and disrupt the biological pathways involved in the growth of cancer. Quinazolin-4(1H)-one derivatives have been studied for anticancer activity by some research groups. Among these agents, Erlotinib, Gefitinib, Afatinib, and Dacomitinib are currently used for the treatment of different types of cancer such as colon, breast, prostate, liver and lung cancer. A quinazolinone -based Schiff base is a compound that combines a quinazolinone ring with a Schiff base (imine) group, often synthesized for its diverse pharmacological activities. These compounds show potential as anticancer, anti-inflammatory, antioxidant, antimicrobial, and

antiviral agents, with studies exploring their use in treating diseases like cancer, HIV, and bacterial infections by acting as inhibitors of various intracellular enzymes[1]. The structure can be further modified to enhance these biological effects. They consist of a bicyclic quinazolinone core (a benzene ring fused with a pyrimidine ring) with a Schiff base moiety, typically attached at the N3 position[2]. They are commonly synthesized by the condensation reaction of a 3-amino-quinazolin-4(3H)-one derivative with various aldehydes or ketones, often under slightly acidic conditions or using microwave-assisted methods[3]. The formation of the imine bond is confirmed by spectroscopic techniques, notably the appearance of a characteristic C=N stretching band around 1600-1630 cm^{-1} in the IR spectrum and specific proton signals in ^{1}H NMR. Quinazolin-4(1H)-one derivatives have been studied for anticancer activity by some research groups. Any Quinazolinone derived Schiff bases and their metal complexes show potent cytotoxic effects against various cancer cell lines, such as breast cancer (MCF-7) and liver cancer (A549) cells[5]. Some induce apoptosis (programmed cell death) via mitochondrial pathways. They display antibacterial and antifungal activities, including efficacy against resistant strains like methicillin-resistant *Staphylococcus aureus* (MRSA),[6]. Research also indicates potential applications as antiviral agents (including potential COVID-19 related targets), anticonvulsants, and antioxidants. Quinazolinone Schiff bases are considered a "privileged scaffold" in drug development due to their stability, relatively simple synthesis, and lipophilicity, which aids in cell membrane penetration[7]. Ongoing research focuses on modifying their structure to develop novel therapeutic agents with improved selectivity and reduced side effects. These compounds are effective against a variety of bacteria, often showing potent activity against both Gram-positive (e.g., *Staphylococcus aureus*, *Bacillus subtilis*) and Gram-negative (e.g., *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella* sp.) strains[8]. Quinazolinone-based Schiff bases exhibit significant antioxidant activity**,** primarily by scavenging free radicals and protecting against oxidative damage[8]. Many of these compounds demonstrate superior efficacy compared to commercial antioxidant standards like ascorbic acid and BHT in *in vitro* assays. A Schiff base[9] (also known as an imine or azomethine) is a class of organic compound defined by the presence of a carbon-nitrogen double bond (C=NC=N C=N), where the nitrogen atom is connected to an alkyl or aryl group, but not hydrogen. They are formed by the condensation reaction of a primary amine with an aldehyde or ketone. Quinazolinone-based Schiff bases are a highly promising area of research in cancer therapy[10], showing significant anticancer activity against various human cancer cell lines, including liver, breast, lung, and colon cancers. Their efficacy often stems from molecular hybridization, where the combined scaffold enhances interactions with biological targets[11].

MATERIALS AND METHODS:

All Solvents and chemicals compounds were purchased from standard suppliers like sigma Aldrich and some were obtained from Lobachemie, JSK Fine and RDH chemicals of analytical grade and were used without further purification. The melting range of the synthesized compounds was performed by LAB-INDIA. MS-VIS Visual melting point apparatus and is uncorrected[12]. The IR spectrum studies of the synthesized compound were recorded by pressed-pellet technique. IR spectra were recorded in KBr press (Shimadzu). The ^{1} H –NMR of the were run on broker NMR machine at 500MHz.the chemical shifts were measured with reference to tetramethylsilane (TMS) and the solvent used were $CDCl_3$ and deuteriated DMSO depending on the solubility properties of the required compound. Chemical shifts are expressed as d (ppm) values. To obtain molecular weight information, quinazolinone derivatives were analyzed by ESI-MS spectrometry. All compounds were routinely checked by TLC on silica gel G plates. the progress of the reaction and the level of purity of the compounds were routinely checked by TLC on silica gel plates using different solvent system based on the variation of polarity of the product of interest and the developed plates were visualized under UV light. All drying was conducted at reduced was conducted in hot air oven.

Synthesis of Quinazolin- 4-one derivatives of Schiff bases (QZT2a-QZT4c)

Synthesis of Benzoxacine-4-One (compound -1)

Equimolar amount of 0.01M of anthranilic acid is dissolved in 1.5ml of acetic anhydride and add drops of pyridine in a RBF. Add sufficient quantity of ethanol[13], stirred the mixture and reflux for 4 hours. The progress of reaction is monitored by

TLC, after the completion of reaction the content of the flask poured into a beaker containing 100ml of cold water to get corresponding benzoxacine-4-one in the solid state[14], showed in Figure 1. The product was further washed, filtered and dried followed by recrystallisation by ethanol.

Synthesis of 2-methyl-4-oxoquinazoline-3(4H)-carboxamide (compound - 2)

A mixture of 2-methyl-4*H*-3,1-benzoxazin-4-one(.03 mol, 4.5 gm) and urea (.03 mol, 4 gm) in glacial acetic acid (30 ml) was mixed thoroughly and transferred in an 250 ml RBF. The mixture was refluxed for 6 hours[15]. The reaction mixture was allowed to cool, filtered by suction, recrystallized by toluene and air-dried to afford moderate to excellent yields of various 2-methyl-3-substituted quinazolin-4(*3H*)-one derivatives (compound 2) which is showed in figure1.

Synthesis of substituted 2-methyl-3-substituted quinazoli-4-one Schiff base derivative (QZT 2a-QZT-2d)

2.47 gm (0.01 mol) 2-methyl-4-oxoquinazoline-3(4H)-caboxamide and add 1.06 gm (0.01 mol) heterocyclic aromatic aldehydes and 2-3 drops of glacial acetic acid in ethanol (30 ml) were placed in 250 ml RBF fitted with reflux condenser and the reaction mixture was stirred well and refluxed for 4-6 hours. The reaction was monitored by TLC. After the completion of the reaction the reaction mixture is poured into a beaker containing cold water and the precipitate of heterocyclic aldehydes derivative was formed[16] showed in figure 1(QZT 2a-QZT-2d). Filter the precipitate and dried well followed by recrystallisation by Ethanol.

Synthesis of 2-methyl-4-oxoquinazoline-3(4H)-carbothioamide (compound - 3)

A mixture of 2-methyl-4*H*-3,1-benzoxazin-4-one(.03 mol, 4.5 gm) and thiourea (.03 mol, 4 gm) in glacial acetic acid (30 ml) was mixed thoroughly and transferred in an 250 ml RBF. The mixture was refluxed for 6 hours. The reaction mixture was allowed to cool, filtered by suction, recrystallized by toluene[17] and air-dried to afford moderate to excellent yields of various 2-methyl-3-substituted quinazolin-4(*3H*)-one derivatives (compound 2) which is showed in figure1.

Synthesis of substituted 2- methyl-3-substituted quinazoli-4-one Schiff base derivative (QZT 3a-QZT-3c)

2.47 gm (0.01 mol) 2-methyl-4-oxoquinazoline-3(4H)-cabothioamide(compound 2) and add 1.06 gm (0.01 mol) heterocyclic aromatic aldehydes and 2-3 drops of glacial acetic acid in ethanol (30 ml) were placed in 250 ml RBF fitted with reflux condenser and the reaction mixture was stirred well and refluxed for 4-6 hours. The reaction was monitored by TLC. After the completion of the reaction the reaction mixture is poured into a beaker containing cold water and the precipitate of heterocyclic aldehydes derivatives (QZT3a-QZT3c) was formed[18] showed in figure1. Filter the precipitate and dried well followed by recrystallisation by Ethanol.

Synthesis of 2-methyl-4-oxoquinazoline-3(4H)-carbothioamide (compound - 4)

A mixture of 2-methyl-4*H*-3,1-benzoxazin-4-one(.03 mol, 4.5 gm) and p-phenylene diamine (.03 mol, 4 gm) in glacial acetic acid (30 ml) was mixed thoroughly and transferred in an 250 ml RBF. The mixture was refluxed for 6 hours[14,19]. The reaction mixture was allowed to cool, filtered by suction, recrystallized by toluene and air-dried to afford moderate to excellent yields of various 2-methyl-3-substituted quinazolin-4(*3H*)-one derivatives (compound 2) as given in figure1.

Synthesis of substituted 2- methyl-3-substituted quinazoli-4-one Schiff base derivative (QZT 4a - QZT-4c)

2.47 gm (0.01 mol) 3-(4-aminophenyl)-2-methylquinazolin-4(*3H*)-one (compound 3) and add 1.06 gm (0.01 mol) heterocyclic aromatic aldehydes and 2-3 drops of glacial acetic acid in ethanol (30 ml) were placed in 250 ml RBF fitted with reflux condenser and the reaction mixture was stirred well and refluxed for 4-6 hours. The reaction was monitored by TLC. After the completion of the reaction the reaction mixture is poured into a beaker containing cold water and the precipitate of heterocyclic aldehyde derivatives (QZT-4a-QZT4c) was formed[15, 20] which is showed in figure1. Filter the precipitate and dried well followed by recrystallisation by Ethanol.

Synthesis of the desired compounds and all the steps were achieved according to the steps illustrated in Figure-1.

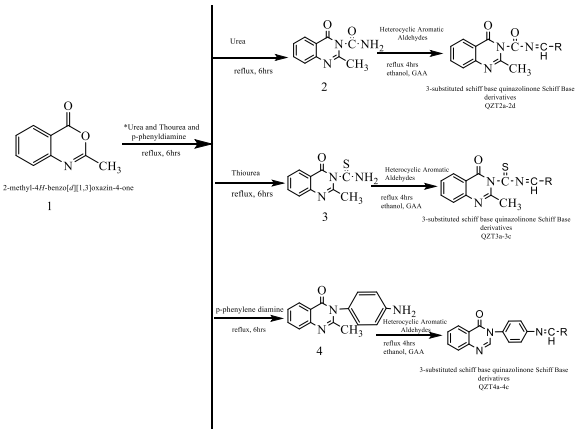
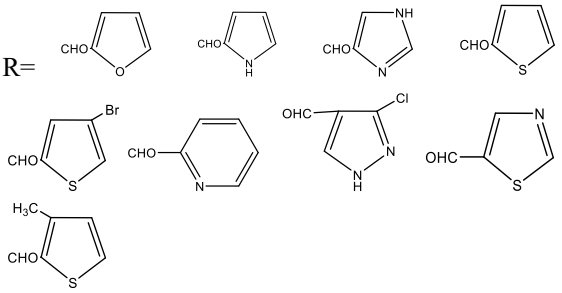


Figure 1: Synthesis of final compounds 2a-4c,*compound QZT 2a-2d(Urea)Scheme-1,QZT 3a-3c(Thiourea)Scheme-2 ,QZT 4a-4c (p-phenylenediamine) Scheme-3 used as reactant.

R=



Physicochemical and spectral Characterization of synthesized derivatives

Thin layer chromatography

Rf value is a characteristic feature of purity of the compound. Thin layer chromatographic analysis of the synthesized compounds was done on silica gel G coated glass plate[21]. All the Rf values mentioned in table 1.

Spectral characterization of synthesized lead compounds

The synthesized lead compounds were confirmed by means of their FT-IR, ^{1}H NMR, and Maas spectrometry. The mass spectra exhibited consecutive intense molecular ion peak m/z [M]+ of titled compounds[22].

PHARMACOLOGICAL ACTIVITY

Anticancer Activity

MTT Assay

The cytotoxicity of the samples provided on cell line (Procured from NCCS Pune) was determined by MTT Assay. The cells (10000 cells/well) were cultured in 96 well plate for 24 h in MEM medium (Minimum Essential Medium Eagle-AT154-1L-HIMEDIA) supplemented with 10% FBS (Fetal Bovine Serum - HIMEDIA-RM 10432) and 1% antibiotic solution (Penicillin-Streptomycin-Sigma-Aldrich P0781) at 37°C with 5% CO_2. Next day cells were treated from different concentrations of the samples (concentration as per mentioned in excel sheet). Stock solution of samples was prepared in DMSO and further diluted to get different concentrations in incomplete Cell culture Medium (Without FBS).After incubation for 24 hours, MTT Solution (5 mg/ml) was added to cell culture and further incubated (Air- jacketed CO2 incubator-Heal force-HF90) for 2 h. Cells without treatment were considered as Control and cells without MTT were considered as Blank[23]. At the end of the experiment, culture supernatant was removed, and cell layer matrix was dissolved in 100 µl Dimethyl Sulfoxide (DMSO–SRL- Cat no.-67685) and read in an Elisa plate reader (iMark, Biorad, USA) at 540 nm. $IC_{50}$was calculated by using Graph Pad Prism -6. Images were captured under inverted microscope (Olympus ek2) using Camera (AmScope digital camera 10 MP Aptima CMOS). 50% inhibitory concentration (IC_{50}) was presented as Mean ± SEM (Standard Error of Mean) [24]. % Viable cells = (A_{test} / $A_{Control}$) *100 where (A_{test} = Absorbance of test sample).

Anti-microbial activity assay

Procurement of Mueller-Hinton Agar (SRL- Chem-Cat no.-24756) (MHA) Plates, Bacterial Culture (*Staphylococcus aureus,* MTCC96 and *Escheriachia Coli,* MTCC 40) from Microbial Type Culture Collection and Gene Bank (MTCC)-Chandigarh. Laboratory reagents were Whatman No 1 filter paper discs (5mm). Solvent (vehicle control)- Dimethyl Sulfoxide - DMSO (SRL Chem 28580) Ciprofloxacin (SRL Chem- 78079)-2mg/ml.

Anti-microbial Assay Procedure

The Antibacterial activity was checked by following Zone Inhibition Method (Kirby-Bauer method). The MHA plates were inoculated by spreading with 100 µl of Bacterial culture, *Staphylococcus aureus* and *Escherichia coli* (Inoculum was prepared by adjusting 0.5 McFarland Unit - Approx cell density (1.5 X 10^8 CFU/mL from Mueller- Hinton Broth) and followed by placing the discs containing 5 µl of different concentration (0 to 200 mM). One disc in each plate was loaded with solvent alone which served as vehicle control and Ciprofloxacin disc (3µg) was taken as positive control[25]. The plates of *Staphylococcus aureus* and *Escheriachia coli* were incubated (Basil Scientific Corp. India) at

37°C for 24 hrs. The clear zones created around the disc were measured and recorded.

Antioxidant Activity

DPPH Scavenging Assay

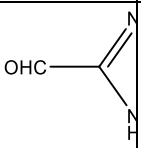
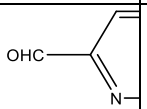
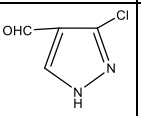
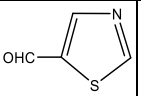
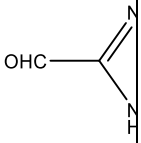
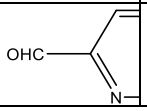
10µl of different stock of the test compound (As per mention in excel sheet) was added to 0.2 ml of 0.1mM DPPH solution (SRL Chem – Cat no.– SR-29128) in Methanol (SD fine- Cat no.- 10930lC250)) in a 96 well plate. Ascorbic Acid – SRL, Cat no- 23006 was used as standard. The reaction was set in quadruplicate form and duplicates of blank were prepared containing 0.2 ml DPPH and 10µl standard/sample of different concentrations (As per mention in excel sheet). The wells without treatment were considered controlled and wells without reagent (DPPH) were considered Blank. The plate was incubated for 30 min in dark. At the end of the incubation, the decolorization was read 517 nm using a micro plate reader (iMark, BioRad). Reaction mixture containing 20µl of deionized water was served as Control. The scavenging activity was presented as '% inhibition' with respect to control[26]. IC_{50} was calculated using Software Graph Pad Prism 6. Graph was prepared between X axis (Sample Concentration) *Vs*. Y axis (% inhibition wrt control). % RSA= $((Abs_{Control}-Abs_{Sample})/Abs_{Control}) \times 100$. Where RSA = Radical Scavenging Activity, $Abs_{Control}$ = Absorbance of control and Abs_{Sample} = Absorbance of sample.

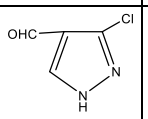
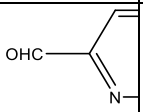
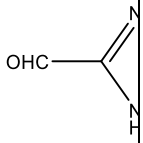
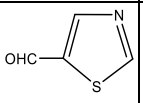
RESULT AND DISCUSSION:

The synthesized lead composed were analyzed for their physical characters viz colour, molecular formula, molecular weight, percentage yield and melting point, log p and Rf and their results were given Table No.1.

Determination of physicochemical properties of Novel Synthesized Compounds

Table 1: Physiochemical Properties of the synthesized Compounds

S.no	Compound Code	Substitution (R)	Colour & Appearance	Molecular Formula	Molecular weight (gm/mol)	Solubility	% Yield	Melting Point (^{0}C)	Rf Value
1.	QZT-2a		Brown solid	$C_{14}H_{11}N_5O_2$	281	H_2O/DMSO	74	228	0.81
2.	QZT-2b		Brown solid	$C_{16}H_{12}N_4O_2$	292	H_2O/DMSO	78	200	0.74
3.	QZT-2c		Brown solid	$C_{14}H_{10}ClN_5O_2$	315	H_2O/DMSO	70	214	0.65
4.1.	QZT-2d		White solid	$C_{15}H_{11}N_3O_2S$	297	H_2O/DMSO	72	201	0.32
5.7.	QZT-3a		Creamish-white solid	$C_{14}H_{11}N_5OS$	297	H_2O/DMSO	72	209	0.34
6.0.	QZT-3b		White solid	$C_{16}H_{12}N_4OS$	308	Ethanol/DMSO	68	146	0.68

7.	QZT-3C		Creamish-white solid	$C_{17}H_{10}ClN_5OS$	331	Ethanol/ DMSO	65	145	0.70
8.	QZT-4a		Creamish-white solid	$C_{21}H_{16}N_4O$	340	Ethanol/ DMSO	71	168	0.74
9.	QZT-4b		White solid	$C_{19}H_{17}N_5O$	331	Ethanol/ DMSO	62	176	0.65
10.	QZT-4C		White solid	$C_{19}H_{14}N_4OS$	346	Ethanol/ DMSO	71	143	0.71

Determination of Anti-cancer activity by MTT Assay

Table 2: In vitro antitumour screening of targeted new compounds 2a-4c against human liver carcinoma cell lines (HepG-2)

Sample code	***IC*$_{50}$value (µg/ml)**
QZT-2a	77.20
QZT-2b	63.03
QZT-2c	51.48
QZT-2d	60.25
QZT-3a	70.18
QZT-3b	24.11
QZT-3c	62.66
QZT-4a	49.19
QZT-4b	61.25
QZT-4c	77.01
Standard 5FU	25.02

Graphical representation of Anti-cancer activity by MTT assay

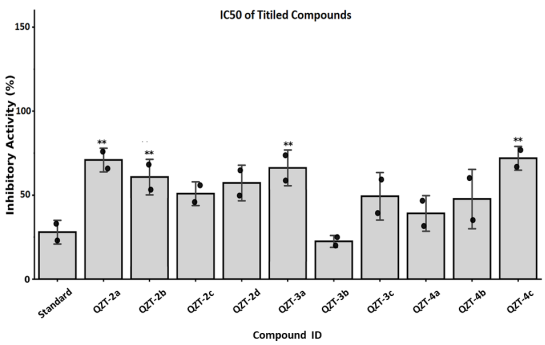


Figure 2: One-Way ANOVA: Comparative Cytotoxic Activity of Quinazolinone Schiff Base Derivatives Against HepG2 Cells (MTT Assay) Bar graph showing IC_{50} values (µg/mL) of synthesized quinazolinone derivatives (QZT-2a to QZT-4c) on HepG2 cell line. Values represent mean ± SEM from triplicate experiments. Bioactivity Comparison l^ * $p < 0.05$ vs Standard **(Mean± SEM)**

Based on the results obtained from the MTT assay, it was observed that when the cell line was exposed to different concentrations of the samples, cytotoxic activity was estimated for all samples and 50% inhibitory concentration as mentioned in table 2. Sample QZT-3b was found to be the most cytotoxic among all the samples, QZT-2c,QZT-2d,QZT-4a and QZT-4b were found to be moderately cytotoxic as compared with standard 5-FU. Bar graph showing IC_{50} values (µg/mL) of synthesized quinazolinone derivatives (QZT-2a to QZT-4c) on HepG2 cell line in Figure 2. *IC_{50}* is the concentration of an inhibitor/sample/ formulation at which the viable cells are reduced by half.

Determination of Anti-microbial activity by Disk Diffusion Method

Table 3: Zone of Inhibition of the synthesized Compounds QZT2a-4c

Compound ID		**Zone of Inhibition (in mm)**	
	Conc. in µg/ml	Staphylococcus aureus	E. coli
Standard	3 µg	24	22

ciprofloxacin			
QZT-2a	125µmol	16	18
QZT-2b	125µmol	6	3
QZT-2c	125µmol	18	20
QZT-2d	125µmol	15	18
QZT-3a	125µmol	4	7
QZT-3b	125µmol	21	20
QZT-3c	125µmol	12	16
QZT-4a	125µmol	17	20
QZT-4b	125µmol	18	13
QZT-4c	125µmol	12	10

Std: ciprofloxacin

Antibacterialactivitywascarriedoutat 3,125 µg/mL

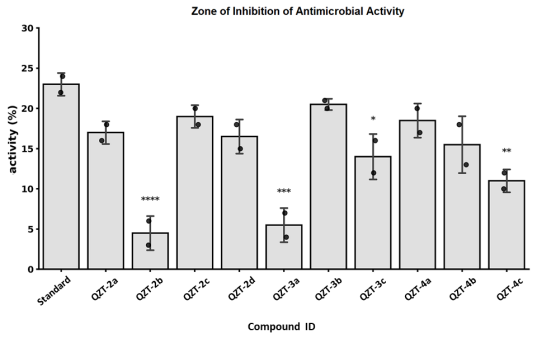


Figure 3: One-Way ANOVA: Comparative antimicrobial Activity of Quinazolinone Schiff Base Derivatives Against bacterial strains by Disk Diffusion method . Bioactivity Comparison l^ * p < 0.05 vs Standard **(Mean± SEM).**

Based on the results obtained from this study, presents a comprehensive one-way Analysis of Variance (ANOVA) comparing the bioactivity of 10 QZT test compounds (at 125 µmol concentration) against a Standard control (at 3 µg concentration). The statistical analysis revealed highly significant differences among the compounds ($F = 16.22$, $p < 0.0001$), with four QZT compounds (QZT-2b, QZT-3a, QZT-3c, and QZT-4c) demonstrating significantly lower activity compared to the Standard. Notably, QZT-3b and 4a emerged as the top-performing test compound with a mean activity of 20.5%, on both the bacteria gram positive staphylococcus aureus and gram negative Escherchia. Coli, approaching the Standard's performance of 23.0%. QZT-2a,QZT-2c,QZT-2d and QZT-4b were found moderate effective at the amount mentioned in the above table – 3 and in figure 2 . The findings suggest that the investigated compounds possess potential activity, as promising candidates for further exploration in the quest for new derivatives with an enhanced overall biological profile.

Determination of Antioxidant activity by DPPH

Table 4: DPPH Scavenging *IC₅₀* value of the synthesized Compounds QZT2a-QZT 4c

Compound ID	***IC₅₀* value** (µg/ml)
Ascorbic Acid	5.5
QZT-2a	32
QZT-2b	46
QZT-2c	5
QZT-2d	40
QZT-3a	35
QZT-3b	3.1
QZT-3c	61
QZT-4a	4
QZT-4b	49
QZT-4c	35

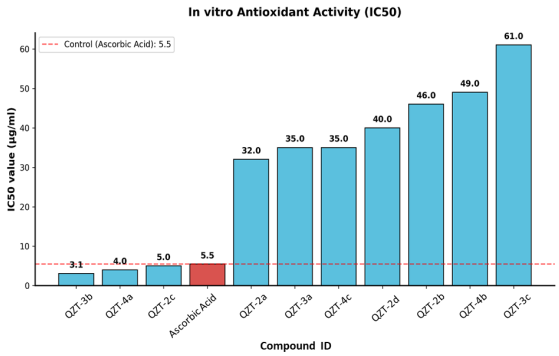


Figure 4:Graph showing antioxidant activity

Antioxidant activity : Based on the results obtained from the experimental work, Antioxidant activity (DPPH Assay) was estimated in 10 test compounds (QZT-2a-QZT-4c) against standard control, Ascorbic acid and 50% inhibitory concentration (*IC₅₀*) were mentioned in table 4 and in figure 4. Sample QZT-3b (3.1 µg/ml) was found to be highly active among all the samples, whereas QZT-4a (4.0 µg/ml), QZT-2c (5.0 µg/ml) was found equivalent to 5.5µg of standard Ascorbic acid.

Spectroscopic Characterization of Synthesized Compounds

The results of the infrared analysis was carried out using JASCO 4100 Fourier- Trasnform Infrared (FT-IR) and the various absorption bands from stretching and bending vibrational frequencies were duly reported. The results of the infrared spectral data of all the synthesized compounds were

presented in the experimental section. The 1H-NMR of the reactive intermediate and targeted novel 3-substituted quinazolinone derived Schiff base motifs QZT 2a-4c were run in either DMSO-d6 or CDCl3 depending on the solubility behaviour of each of the compound to be analyzed per time. The complete spectroscopic characterization of synthesized compounds (QZT 2a-QZT 4c) were explained below:

QZT-2a IR (ranges in cm^{-1}) :3477 (N-H stretching), 2890 (C-H aldehyde stretching), 2820 (C-stretching), 2852(C-H stretching), 1609 (C=O stretching), 1642 (C=C stretching), 1465 (C-H bend.), 1460 (C-H bend.), 1053 (C-C str.), 739 (CH_2 rocking), **^{1}HNMR** (DMSO): δ 6.24-7.28 (m, 1H, H-6), δ 4.57 (s, 1H), δ 4.14 (s, 1H), 3.20 (tdd, CH_3, H-3), δ 1.23 (s, 3H), δ 1.19 (s, 3H), δ 1.06 (s, 3H), δ 0.98 (s, 3H), δ 0.91 (s, 3H). **EI MS**: 228 [$M^+C_{14}H_{11}N_5O_2$], 210

QZT-2b IR (ranges in cm^{-1}) :3487(N-H stretching), 3412 (N-H stretching), 2877 (C-H aldehyde stretching), 2840 (C-stretching), 2847 (C-H stretching), 1620 (C=O stretching), 1652 (C=C stretching), 1413(C-H bend.), 1428(C-H bend.), 1060 (C-C str.), 730 (CH_2 rocking), **^{1}HNMR** (DMSO): δ 7.03-7.92 (m, 1H, H-6), δ 4.23 (s, 1H), δ 4.17 (s, 1H), 3.56 (t, CH_3, H-3), δ 1.16 (s, 3H), δ 1.15(s, 3H), δ 1.02 (s, 3H), δ 0.96 (s, 3H), δ 0.93 (s, 3H). **EI MS**: 292 [M^+ $C_{16}H_{12}N_4O_2$]

QZT-2c IR (ranges in cm^{-1}) :3422 (N-H stretching), 3418 (N-H stretching), 2863 (C-H aldehyde stretching), 2846 (C-stretching), 2840 (C-H stretching), 1617 (C=O stretching), 1650 (C=C stretching), 1403(C-H bend.), 1419 (C-H bend.), 1055 (C-C str.), 729 (CH_2 rocking), **^{1}HNMR** (DMSO): δ 6.98-8.02 (m, 1H, H-6), δ 4.21 (s, 1H), δ 4.15 (s, 1H), 3.50 (t, CH_3, H-3), δ 1.11 (s, 3H), δ 1.10(s, 3H), δ 1.05 (s, 3H), δ 0.94 (s, 3H), δ 0.91 (s, 3H). **EI MS**: 329 [M^+ $C_{14}H_{11}N_5O_5$].

QZT-2d IR (ranges in cm^{-1}) :3458 (N-H stretching), 3421 (N-H stretching), 2822 (C-H aldehyde stretching), 2819 (C-stretching), 2816 (C-H stretching), 1623 (C=O stretching), 1644 (C=C stretching), 1413(C-H bend.), 1416 (C-H bend.), 1063 (C-C str.), 720 (CH_2 rocking), **^{1}HNMR** (DMSO): δ 7.09-7.88 (m, 1H, H-6), δ 4.19 (s, 1H), δ 4.11 (s, 1H), 3.48 (t, CH_3, H-3), δ 1.10 (s, 3H), δ 1.09 (s, 3H), δ 1.01 (s, 3H), δ 0.92(s, 3H), δ 0.90 (s, 3H). **EI MS**: 308 [M^+ $C_{14}H_{11}N_5O_5$]

QZT-3a IR (ranges in cm^{-1}) :3356 (N-H stretching), 3403 (N-H stretching), 2910 (C-H aldehyde stretching), 2906 (C-stretching), 2823 (C-H stretching), 1712 (C=O stretching), 1630 (C=C stretching), 1409 (C-H bend.), 1400 (C-H bend.), 1028 (C-C str.), 718 (CH_2 rocking), **^{1}HNMR** (DMSO): δ 6.77-7.72 (m, 1H, H-6), δ 5.12 (s, 1H), δ 4.03 (s, 1H), 3.20 (t, CH_3, H-3), δ 1.09 (s, 3H), δ 1.01 (s, 3H), δ 1.00 (s, 3H), δ 0.96(s, 3H), δ 0.95 (s, 3H). **EI MS**: 328 [M^+ $C_{20}H_{16}N_4O$]

QZT-3b IR (ranges in cm^{-1}) :3290 (N-H stretching), 3378 (N-H stretching), 2923 (C-H aldehyde stretching), 2815 (C-stretching), 2879 (C-H stretching), 1716 (C=O stretching), 1610 (C=C stretching), 1420 (C-H bend.), 1428 (C-H bend.), 1087 (C-C str.), 762 (CH_2 rocking), **^{1}HNMR** (DMSO): δ 7.25-8.02 (m, 1H, H-6), δ 4.16 (s, 1H), δ 4.13 (s, 1H), 3.47 (t, CH_3, H-3), δ 1.13 (s, 3H), δ 1.11(s, 3H), δ 1.09 (s, 3H), δ 0.98(s, 3H), δ 0.91 (s, 3H). **EI MS**: 339 [M^+ $C_{22}H_{17}N_3O$] .

CONCLUSION:

In conclusion, we have synthesized a series of 2-methyl,3-substituted quinazolinone derived Schiff base reacted with different nitrogen nucleophiles substituted with various heterocyclic aldehydes. Of all the compounds synthesized, compounds QZT-3b showed a potent cytotoxic compound among them compound QZT-2c, QZT-2d, QZT-4a and QZT-4b exhibited moderately active cytotoxic novel compounds against HepG2 cancer cell lines, Based on the results obtained from the MTT assay, it was observed that when the cell line was exposed to different concentrations of the samples, cytotoxic activity was estimated for all samples and 50% inhibitory concentration. Sample QZT-3b and 4a was found most potent anti-microbial activity ,among them QZT-2d,2c,2d and 4b demonstrated as moderately containing antimicrobial activity compared with standard by disk diffusion method against staphylococcus aureus and Escherichia coli. Based on the results obtained from the experimental work, Antioxidant activity (DPPH Assay) was estimated in sample QZT-3b,4a and 2c showed 50% inhibitory concentration (IC_{50}) were mentioned in table 4.Sample QZT-3b was found to be highly active among all the samples.

Conflict of interest: Nil

REFERENCES:

1. Hricovíniová Z, Hricovíni M, Kozics K. New series of quinazolinone derived Schiff's bases: Synthesis, spectroscopic properties and evaluation of their antioxidant and cytotoxic activity. Chemical Papers. 2018 ;72(4):1041-1053.

2. Besson T, Chosson E. Microwave-assisted synthesis of bioactive quinazolines and quinazolinones. Combinatorial Chemistry & High Throughput Screening. 2007;10(10):903-917.

3. Aziz MW, Kamal AM, Mohamed KO, Elgendy AA. Design, synthesis and assessment of new series of quinazolinone derivatives as EGFR inhibitors along with their cytotoxic evaluation against MCF7 and A549 cancer cell lines. Bioorganic & medicinal chemistry letters.2021;41:127-134.

4. Martins P, Jesus J., Santos S., Raposo L.R., Roma-Rodrigues C., Baptista P.V., Fernandes A. R., Heterocyclic anticancer compounds: recent advances and the paradigm shift towards the use of nano medicine's tool box, Molecules 20,2015 16852–16891.

5. Qureshi SI, Chaudhari HK. Design, synthesis, in-silico studies and biological screening of quinazolinone analogues as potential antibacterial agents against MRSA. Bioorganic & Medicinal Chemistry. 2019 ;27(12):2676-88.

6. Kushwaha N, Sahu A, Mishra J, Soni A, Dorwal D. An insight on the prospect of quinazoline and quinazolinone derivatives as anti-tubercular agents. Current Organic Synthesis. 2023 ;20(8):838-69.

7. Chevalier J, Mahamoud A, Baitiche M, Adam E, Viveiros M, Smarandache A, Militaru A, Pascu ML, Amaral L, Pagès JM. Quinazoline derivatives are efficient chemosensitizers of antibiotic activity in Enterobacter aerogenes, Klebsiella pneumoniae and Pseudomonas aeruginosa resistant strains. International journal of antimicrobial agents. 2010 ;36(2):164-8.

8. Hricovíniová J, Hricovíniová Z, Kozics K. Antioxidant, cytotoxic, genotoxic, and DNA-protective potential of 2, 3-substituted quinazolinones: Structure—Activity relationship study. International Journal of Molecular Sciences. 2021;22(2):610.

9. Gurgul I, Hricovíniová J, Mazuryk O, Hricovíniová Z, Brindell M. Enhancement of the cytotoxicity of quinazolinone Schiff base derivatives with copper coordination. Inorganics. 2023;11(10):391.

10. Tokalı FS. Recent advances in quinazolinone derivatives: structure, design and therapeutic potential. Future Medicinal Chemistry. 2025;17(9):1071-91.

11. Tokalı FS. Recent advances in quinazolinone derivatives: structure, design and therapeutic potential. Future Medicinal Chemistry. 2025 May 3;17(9):1071-91.

12. Đilović I, Judaš N, Komar M, Molnar M, Počkaj M, Balić T. Impact of Molecular and Crystal Structure on the Melting Points in Halo-Substituted Phenyl-Quinazolinones. Crystals. 2024;15(1):39.

13. Wang X, Yin J, Shi L, Zhang G, Song B. Design, synthesis, and antibacterial activity of novel Schiff base derivatives of quinazolin-4 (3H)-one. European journal of medicinal chemistry. 2014 ;77:65-74.

14. Dewangan D, Nakhate KT, Verma VS, Nagori K, Tripathi DK. Synthesis, characterization, and screening for analgesic and anti-inflammatory activities of schiff bases of 1, 3, 4-oxadiazoles linked with quinazolin-4-one. Journal of Heterocyclic Chemistry. 2017 ;54(6):3187-94.

15. Parmar MB, Vara MK, Pandya JH. A brief review on imidazole, triazine, and isatin derivatives: synthesis approaches and their applications. Discover Chemistry. 2024 Nov 26;1(1):56.

16. Malik S, Bahare RS, Khan SA. Design, synthesis and anticonvulsant evaluation of N-(benzo [d] thiazol-2-ylcarbamoyl)-2-methyl-4-oxoquinazoline-3 (4H)-carbothioamide derivatives: A hybrid pharmacophore approach. European Journal of Medicinal Chemistry. 2013;67:1-3.

17. Z Shawer T, M El-Sehrawi H, E Mansour R. Design, Synthesis, QSAR, Molecular Docking Study and Antitumor Activity of some Novel Quinazolin-4 (3H)-One Derivative. Journal of Pharmaceutical and Applied Chemistry. 2016 1;2(1):1-4.

18. Al-Abdullah ES, Al-Tuwaijri HM, Hassan HM, Al-Alshaikh MA, Habib EE, El-Emam AA. Synthesis, antimicrobial and hypoglycemic activities of novel N-(1-adamantyl) carbothioamide derivatives. Molecules. 2015 6;20(5):8125-43.

19. Gineinah MM, El-Sherbeny MA, Nasr MN, Maarouf AR. Synthesis and Antiinflammatory Screening of Some Quinazoline and Quinazolyl-4-oxoquinazoline Derivatives. Archiv der Pharmazie: An International Journal Pharmaceutical and Medicinal Chemistry. 2002 ;335(11-12):556-62.

20. Huan LC, Anh DT, Truong BX, Duc PH, Hai PT, Duc-Anh L, Huong LT, Park EJ, Lee HJ, Kang JS, Tran PT. New Acetohydrazides

Incorporating 2-Oxoindoline and 4-Oxoquinazoline: Synthesis and Evaluation of Cytotoxicity and Caspase Activation Activity. Chemistry & Biodiversity. 2020 ;17(3):e1900670.

21. Tran PT, Phuong CV, Duc PH, Anh DT, Hai PT, Huong LT, Thuan NT, Lee HJ, Park EJ, Kang JS, Linh NP. Novel 3, 4-dihydro-4-oxoquinazoline-based acetohydrazides: Design, synthesis and evaluation of antitumor cytotoxicity and caspase activation activity. Bioorganic Chemistry. 2019 1;92:103202.

22. Naziri M, Mokhtary M, Safa F. New substituted quinazoline analogs: Synthesis, anticancer evaluation and docking study. Journal of Molecular Structure. 2023 Apr 15;1278:134915.

23. Sharma KK, Kumar G, Devi S, Kumar G. Synthesis of Some Thiazolyl and Oxazolyl Quinazoline Derivatives as Potential Anti-Microbial Agents. Current Organic Synthesis. 2025 Jul;22(5):639-48.

24. Obafemi CA, Fadare OA, Jasinski JP, Millikan SP, Obuotor EM, Iwalewa EO, Famuyiwa SO, Sanusi K, Yilmaz Y, Ceylan Ü. Microwave-assisted synthesis, structural characterization, DFT studies, antibacterial and antioxidant activity of 2-methyl-4-oxo-1, 2, 3, 4-tetrahydroquinazoline-2-carboxylic acid. Journal of Molecular Structure. 2018, 5;1155:610-22.