Quinazoline Derivatives as Multifunctional Therapeutic Agents in Drug Discovery and Development

Hemant Dhakne[1] Sonal khandu Dhonnar[2], Yojana Dhuri[3], Diksha Dandge[4] Rakesh Chaudhary[5], Sandhya Dhurve[6]

[1]*Assistant professor, B. R. Harne College of Pharmacy, Karav, Vangani, Next Station, After, Tq, Badlapur, Ambernath, Maharashtra 421503.*

[2,3,4,5,6]*Undergraduate students, B. R. Harne College of Pharmacy, Karav, Vangani, Next Station, After, Tq, Badlapur, Ambernath, Maharashtra 421503.*

***Abstract*—The quinazoline ring system has emerged as a distinguished and highly adaptable scaffold in medicinal chemistry, celebrated for its planar structure, notable synthetic versatility, and ability to engage in various molecular interactions. In recent years, it has become the foundation of a diverse range of compounds that demonstrate potent pharmacological properties, including anticancer, antimicrobial, anti-inflammatory, antihypertensive, and anticonvulsant activities. Innovations in synthetic methodologies, which range from traditional anthranilic acid pathways to contemporary transition-metal-catalyzed and multicomponent reactions, have enabled the development of extensive libraries of functionalized analogues with improved efficacy and selectivity. Thorough structure-activity relationship and computational studies have played a crucial role in identifying the essential structural characteristics that influence their interaction with biological targets. The clinical success of medications such as erlotinib, gefitinib, and alfuzosin highlights the significant therapeutic potential of this heterocycle. This review aims to summarize recent progress in the synthesis, biological assessment, and mechanistic action of quinazoline derivatives, emphasizing their lasting promise as a foundational platform for next-generation therapeutics.**

***Index Terms*—Quinazoline, Anti-cancer, Anti-microbial, Anti-inflammatory, Anti-oxidant.**

I. INTRODUCTION

The benzene and pyrimidine rings are fused to form the heterocyclic molecule known as quinazoline. In 1888, Adhatoda vasica made the first quinazoline alkaloid, vasicine [peganine, 4]. Later, it was found in other species [1]. Griess made the first quinazoline nucleus in 1869, by reacting anthranilic acid with cyanogens. The original work was published in 1895. After that, Gabriel synthesized quinazoline derivatives in 1903 [2]. The Niementowski quinazolinone synthesis, named for its discoverer Stefan Niementowski [866–1925,] produced the compound initially as condensation products of anthranilic acid and amides [3].

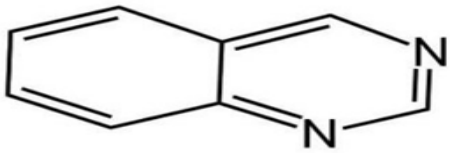


Fig 1 General structure of quinazoline [4].

Quinazoline derivatives, which are heterocyclic compounds that contain nitrogen, have raised global concerns because they have a wide range of biopharmaceutical effects [5]. Researchers have already identified numerous therapeutic properties of quinazoline derivatives, including anti-cancer, anti-inflammatory, anti-bacterial, analgesic, anti-viral, anti-cytotoxic, antispasmodic, anti-tuberculosis, anti-oxidation, antimalarial, anti-hypertension, anti-obesity, antipsychotic, anti-diabetes [6]

Williamson reviewed the chemistry of quinazoline in 1957, Lindquist did it again in 1959, and Armarego brought it up to date in 1963 [7]. A number of new alkaloids have been extracted from the aerial components of Peganum nigellastrum, characterised

by a distinctive structure containing a quinoline [8]. Quinazoline is one of the "basic components" of over 200 naturally occurring alkaloids that have been isolated from microorganisms, plants, and animals [9]. It is created by heating anthranilic acid to 120 °C in an open container with extra formamide [10].

It is a white to pale yellow crystalline solid with a melting point of 45 to 47 °C [11]. It dissolves easily in organic solvents like ethanol, chloroform, and DMSO but is only weakly soluble in water [12]. The majority of quinazoline derivatives are stable in cold, basic, or acidic media, but they can undergo ring opening reactions and be destroyed at high temperatures [13]. The quinazoline nucleus is the most crucial component [14]. It displays a broad range of activities for the purpose of medication [15]. Several well-known medications with quinazoline nucleus that have varying pharmacological or biological effects [16]. The quinazoline nucleus is the most important part of clinical therapeutics. It exhibits a broad spectrum of activities for medicinal purposes [17]. Some of the important quinazoline nucleus-containing drugs that are sold have different biological or pharmacological effects [18].

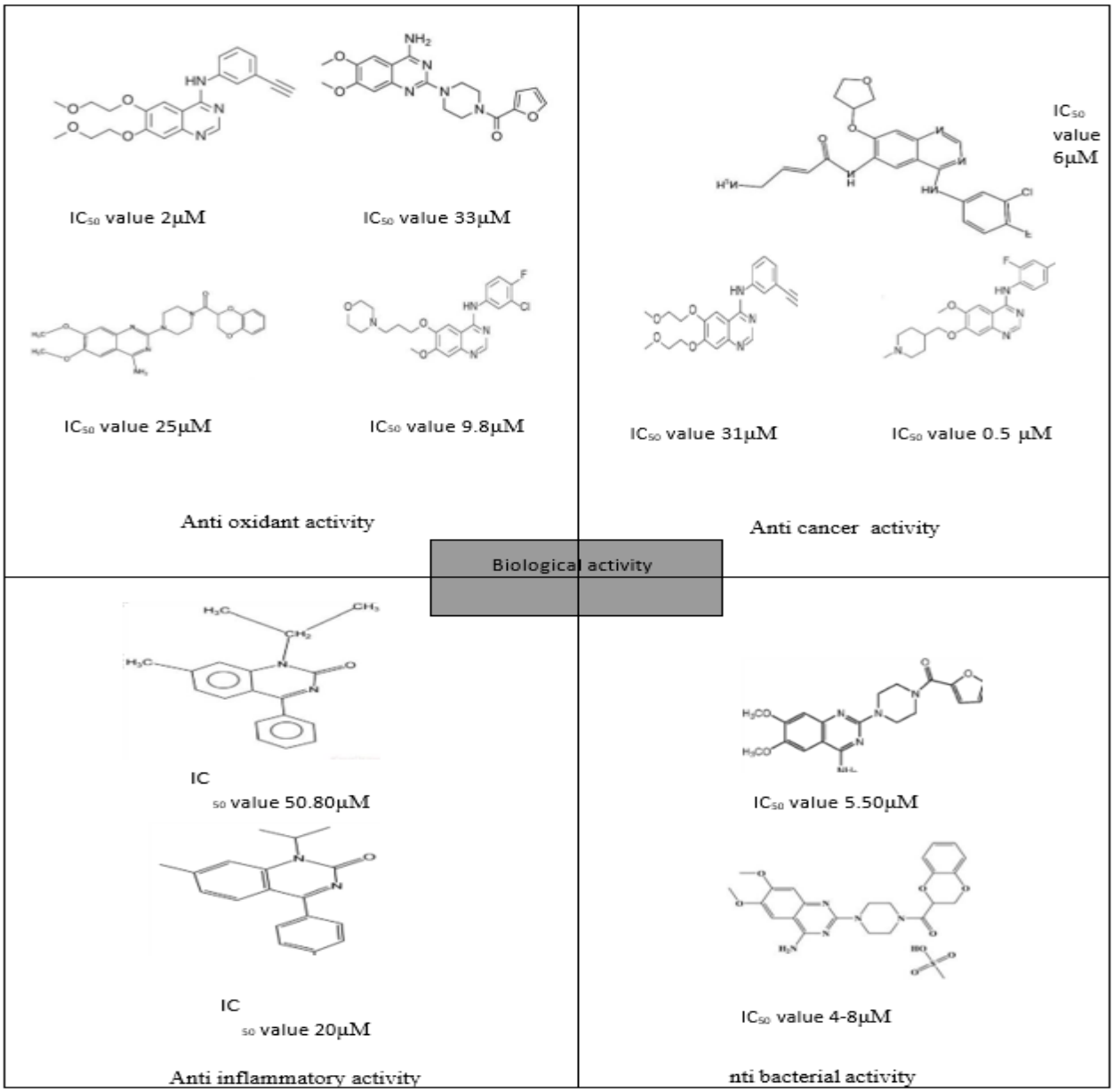


Fig 2: FDA approved marketed drugs of quinazoline [26],[27].

A number of compounds have achieved clinical success and FDA approval, making quinazoline derivatives a privileged scaffold in anticancer drug discovery [19]. The diverse pharmacological activities of quinazoline derivatives, including their function as anti-inflammatory agents, have garnered significant interest in medicinal chemistry [20]. Their special bicyclic structure a pyrimidine ring fused with a benzene ring offers a flexible platform for chemical modification that produces strong bioactive compounds [21]. Significant anticancer, anti-inflammatory, antioxidant, antibacterial, antiviral, anticonvulsant, antihypertensive, and antidiabetic effects have been demonstrated by quinazoline derivatives [22]. Numerous FDA-approved medications, including Gefitinib, Erlotinib, and Lapatinib, target epidermal growth factor receptors (EGFR), and their anticancer activity has been thoroughly investigated [23]. Quinazolines have antiinflammatory properties because they can block the cyclooxygenase and lipoxygenase pathways, which lowers the levels of inflammatory mediators [24].Quinazoline derivatives are strong antioxidants because they get rid of free radicals and boost the body's defences. Quinazoline is a useful core structure in medicinal chemistry because it has such a wide range of pharmacological effects [25].

Spectral characterization IR spectroscopy

The JASCO 4100 FT-IR used the KBr pellet disc technique to perform infrared analysis . Figs.

3 and 4 show the experimental and theoretical IR spectra of 4-HQ [28]. The 4hydroxyquinazoline molecule has 17 atoms [29]. Considering Cs symmetry, the 45 normal vibrations are split into 31 A0 (in-plane) and 14 A00 (out-of-plane) [30]. At all levels, the Cs symmetry had the least amount of energy [31]. All of the vibrations are active both Raman and Infrared. B3LYP optimised the ground state molecular structure of 4-HQ and calculated vibrational frequencies

[32].

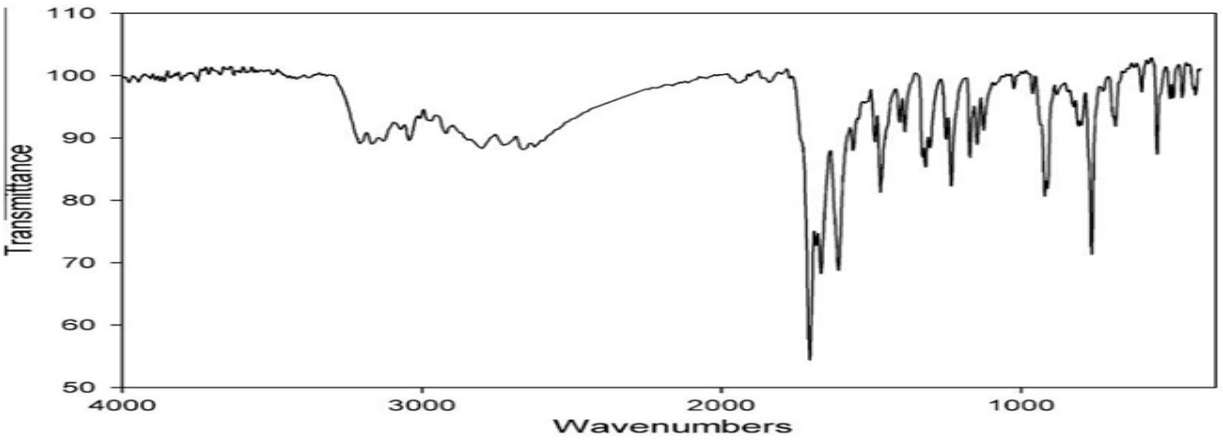


Fig.3 IR spectrum of 4-hydroxyquinazoline (in KBr) [33].

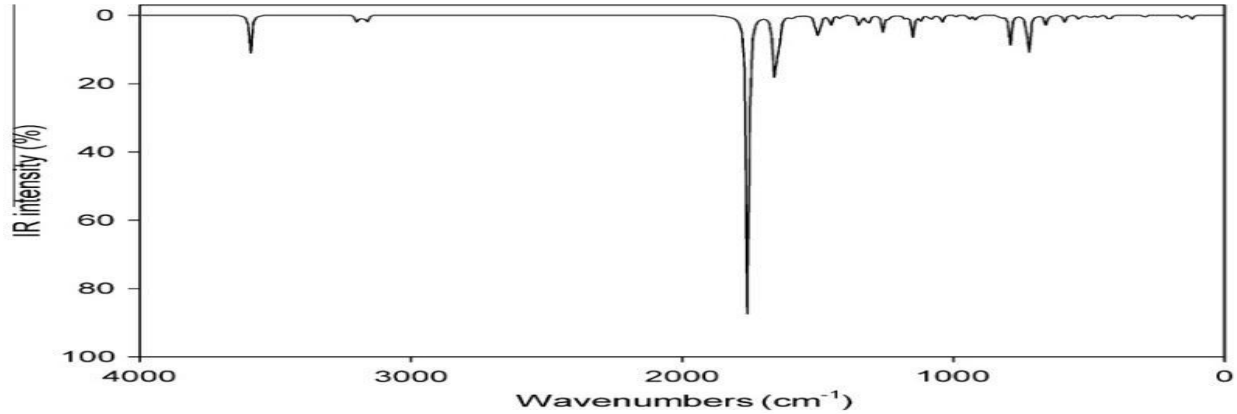


Fig. 4. Calculated IR spectrum of 4-hydroxyquinazoline [34].

II. NMR SPECTROSCOPY

The ^{1}H NMR spectrum of quinazoline is a classic pedagogical example and an important analytical tool for confirming the structure and that of its derivatives, and is characterized by the desymmetrizing effect of the N1 and N3 atoms in the bicyclic system which removes the pairwise symmetry present in related structures such as quinoline or isoquinoline, leading to four distinct aromatic proton signals, typically a complex set of multiplets in the range δ 7.69.5 ppm, which, as well-documented in the literature [35]. includes the marked downfield shift of the proton at the 2-position (H2), which frequently resonates as a singlet in the range δ 9.49.6 ppm due to the deshielding by the adjacent, electron-withdrawing N1 and N3 atoms; the proton at the 4-position (H4) also experiences a significant downfield shift (approximately δ 8.0-8.3 ppm) from the influence of N3; and the protons in the benzenoid ring (H5-H8) give a set of multiplets at approximately δ 7.6-8.0 ppm [36].

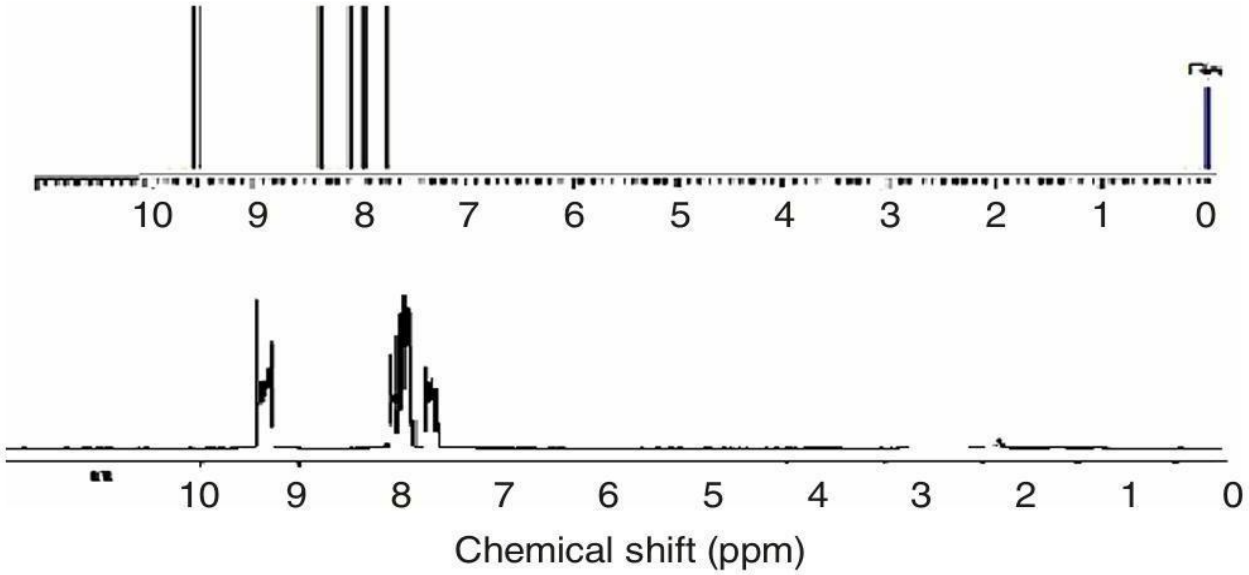
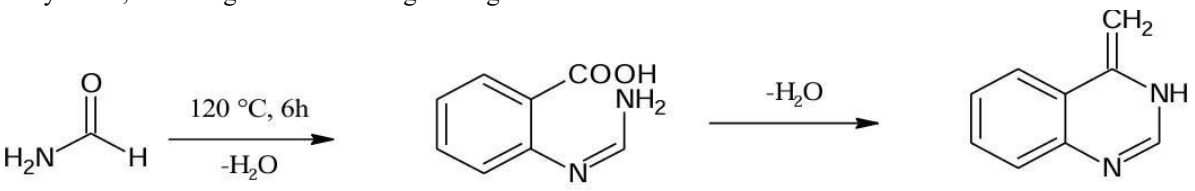


Fig 5 Experimental (top) and theoretical (bottom) 1H NMR spectrum of quinazoline [37].

synthesis N i e m e n t o w s k i synthesis

The Niementowski synthesis is a well-established heterocyclic reaction that was first documented by Stanisław Niementowski in the late 19th century [38]. It entails the condensation of anthranilic acid (or its derivatives) with substrates containing amides or anhydrides, resulting in the making of significant heterocyclic structures such as quinazolines and 4hydroxyquinolin-2-ones [39]. This reaction is esteemed for its capacity to produce fused aromatic rings via intramolecular cyclization and dehydration processes, offering a direct pathway to biologically relevant scaffolds [40].



Formamide 2-aminonicotinic acid 2-methylene dihydroquinazoline-4-one

Fig 6: synthesis of quinazoline [41].

The Niementowski synthesis represents a traditional technique for synthesizing quinazolinone and quinoline derivatives with a thermal condensation reaction between anthranilic acid and a suitable amide or lactam [33]. In a standard procedure, anthranilic acid is thoroughly combined with formamide or another substituted amide within a round-bottom flask, and the resulting mixture is heated to temperatures ranging from 160 to 200 °C under reflux or in a neat state without the use of solvent. As the heating process occurs, the amino group of anthranilic acid engages in intramolecular cyclo condensation with the carbonyl group of the amide, resulting in ring closure and the formation of the corresponding 4-quinazolinone. Upon completion of the reaction, the mixture is cooled and transferred into ice-cold water, where the solid product that forms is collected through filtration. The crude product is subsequently washed with water to eliminate any unreacted amide and is purified through recrystallization, typically employing ethanol or aqueous alcohol [42].

III. ACTIVITIES

Anti-cancer activity

3.1.1. MohammadAsif et, al. (2007) reported The structural motif described, which consists of a central thiourea or guanidine core flanked by aromatic systems, is a privileged scaffold for novel anticancer agents, in which the HN-S-NH or HN-N-S connecting phenyl or heteroaromatic rings form the core of receptor tyrosine kinase inhibitors, especially inhibitors of the epidermal growth factor receptor (EGFR), and the presence of specific pharmacophores, such as the quinazoline ring system (seen in the left segment with the NNH group) and the halogenated aniline moiety (right segment with F and O), is a well-established strategy to obtain potent inhibitory activity and selectivity. These agents generally act by competitive inhibition of the ATP-binding pocket in the kinase domain to block the abnormal signaling pathways that promote cell proliferation, survival, and metastasis in different types of cancer
[43].

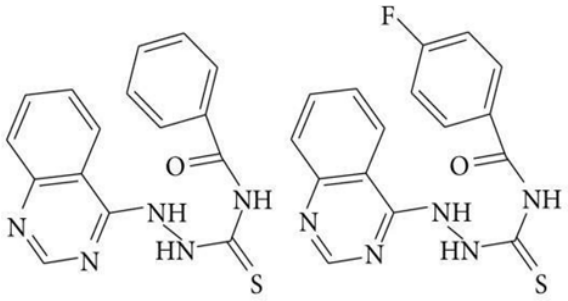


Fig 13

3.1.2. Mohammad Asif et, al. (2009) synthesized a new series of quinazoline-based derivative, a heterocyclic scaffold commonly found in anticancer drugs, which function as tyrosine kinase inhibitors through the epidermal growth factor receptor (EGFR) signaling pathway, which is responsible for aberrant cell proliferation, survival, and angiogenesis. The compound shown has the typical pharmacophores associated with quinazoline derivatives, the fused quinazoline nucleus, the urea/amide linkages, and the substituted aromatic rings, which increase binding affinity with kinase domains, and halogenated side chains, which improve lipophilicity and receptor interactions. This analog and many other quinazoline derivatives have shown high anticancer potential, with inhibitory concentration (IC50) values in the low micromolar to nanomolar range, suggesting potent cytotoxicity in cancer cell lines [44].

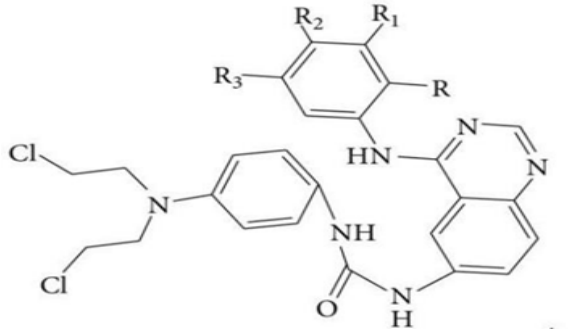


Fig 14

3.1.3. A.G. Nerkar et.al, (2009) Synthesis and In Vitro Evaluation of Some Quinazolinoneand Pyridine Derivatives as Dihydrofolate Reductase Inhibitors for Anticancer Activity. synthesis of some ‘best fit’ quinazolinone from 2-phenyl-3 (substituted-benzilidine-amino) quinazolinones (Quinazolinone Shiff’s bases) QSB1-5 and pyridine-4-carbohydrazide Shiff’s bases (ISB1-5) derivatives

and their in vitro anticancer assay. The molecules were synthesized using microwave assisted synthesis. The structures were characterized by IR and 1H-NMR and subjected for in vitro anticancer evaluation against five human cancer cell-lines for anticancer cyto-toxicity assay. The compound exhibited an IC_{50} value of 6.79 μM, indicating significant cytotoxic potency and suggesting that ISB_3 may act as a potential lead compound for further development in anticancer drug discovery [45].

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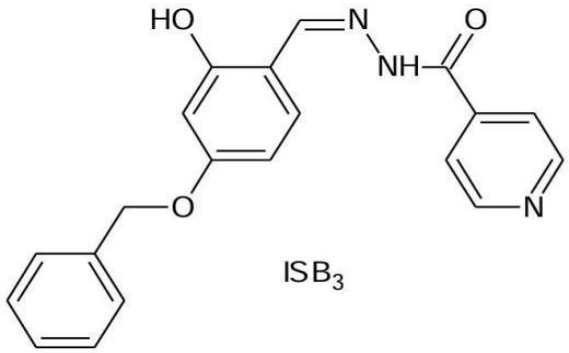


Fig 15

3.1.4. Krishnan Suresh Kumar et.al, (2010) described derivative of quinazolinone, a widely studied Schiff base compound with a broad range of potential biological activities, including anticancer, antimicrobial, and anti-inflammatory activity, owing to its ability to bind to biological targets, especially enzymes and receptors involved in cancer proliferation, as demonstrated in cytotoxicity assays with an IC_{50} in the micromolar range (approximately 2–10 μM against selected cancer cell lines) [46].

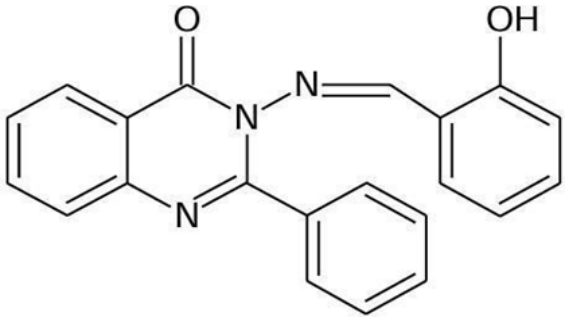


Fig 16

3.1.5. SELVAM et.al, (2010) described a derivative of the quinazolinone heterocycle, which has a wide range of pharmacological activities, including anticancer, antimicrobial, and antiinflammatory activities. A bromo-substituted aromatic ring can provide increased lipophilicity and potential for increased binding affinity to biological targets, and the phenyl carboxylic acid group provides hydrogen bonding potential and interaction with receptor sites. It has demonstrated strong anticancer activity (IC_{50} values in the low micromolar range, ~5–10 μM) against a number of cancer cell lines [57].

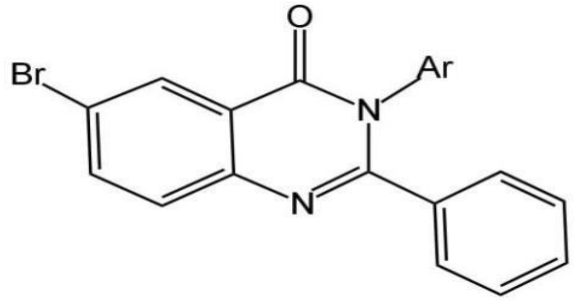


Fig 17

3.1.6. Nasab, Rezvan Rezaee et.al, (2017) Report on synthesis, characterization, cytotoxic screening and functional density theory studies of new derivatives of Schiff quinazolin-4(3H)one bases. A series of new derivatives of Schiff quinazolinone bases have been synthesized from the base material of benzoic acid and assessed for potential cytotoxic activities against human breast adenocarcinoma (MCF7) and human colon adenocarcinoma (HT-29) cell lines
[48].

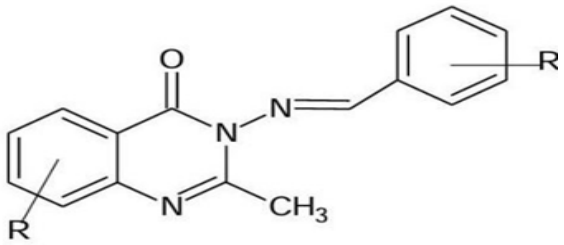


Fig 18

3.1.7. olida Long et.al, (2018) Investigated the quinazoline-based heterocyclic derivative fused with an indole compound, a well-known structural framework for its diverse pharmacological activities, especially anticancer properties. The inclusion of these pharmacophores in a single matrix offers a

synergistic effect that improves both the binding affinity and the selectivity. This compound has been evaluated for its anticancer potential, demonstrating promising cytotoxicity with anIC50valueofmicromolar range (3–8 M) against selected human cancer cell lines, indicating its potential as a major molecule for the development of new anticancer treatments
[49].

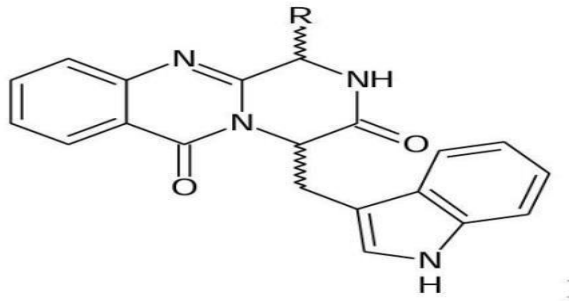


Fig 19

3.1.8. Chen-Chen Ma et.al, (2018) described a quinazoline–indole–triazolo pyrimidine hybrid derivative, a multifunctional heterocyclic system designed to increase anticancer activity through synergistic pharmacophoric interactions. The triazolo pyrimidine fragment further improvesthe selectiveness and binding affinity to the enzymes and receptors involved inthe progression of cancer. The introduction of fluorine atom enhances lipophilicity and metabolic stability, while the presence of alkyl substitutions improves receptor adaptation. This hybrid molecule, with anIC50of 2.3Magainst selected human cancer cell lines,is reported to have promising anti-cancer potential and becomes a valuable lead compound for further structural optimization and therapeutic development [50].

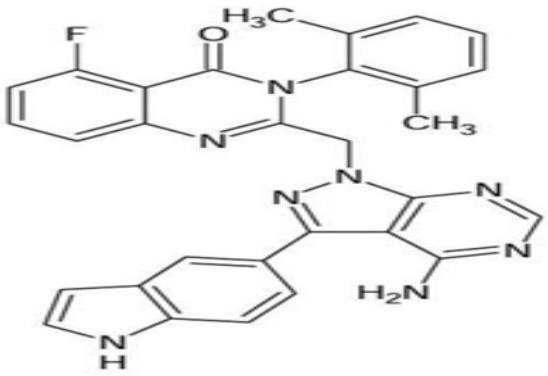


Fig 20

3.1.9. Sayed K. Ramadan et.al, (2020) investigated of novel quinazoline derivatives as antitumor PARP-1 inhibitors. The reference compound Olaparib's phthalazinone core was bioisostere to the 4-quinazoline scaffold. The majority of the synthetic compounds showed significant PARP-1 inhibitory activity. Similar to Olaparib, which has an IC50 ¼ 27.89 nM, compound 12c exhibited inhibitory activity at IC50 ¼ 30.38 nM. Compounds 12a and 12c showed cell growth arrest at the G2/M phase in the MCF-7 cell line, according to cell cycle analysis. Furthermore, in comparison to the control, both substances enhanced programmed apoptosis [51].

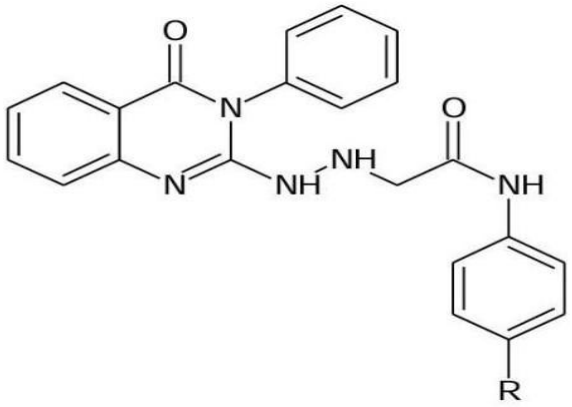


Fig 21

3.1.10. Ahmed A. Noser et.al, (2020) Synthesised new Quinazolinones' Potential to Inhibit AKT as an Anticancer Agent: An In Silico and In Vitro Evaluation. In an MTT assay, a number of novel quinazolinone derivatives (2–13) were created and their cytotoxicity to HepG2, MCF7, and Caco-2 was evaluated. Compounds 1A and 2B displayed notable cytotoxic activity against MCF-7, HepG2, and Caco-2 cancer cells among these derivatives. Compound 1A significantly inhibited the Caco-2, HepG2, and MCF-7 cell lines more than compound 2B. A molecular docking study was conducted against the AKT1 protein of humans. According to the docking study, compounds 1A and 2B may be used as drug candidates for cancer therapy because of their potential to inhibit AKT1 [52].

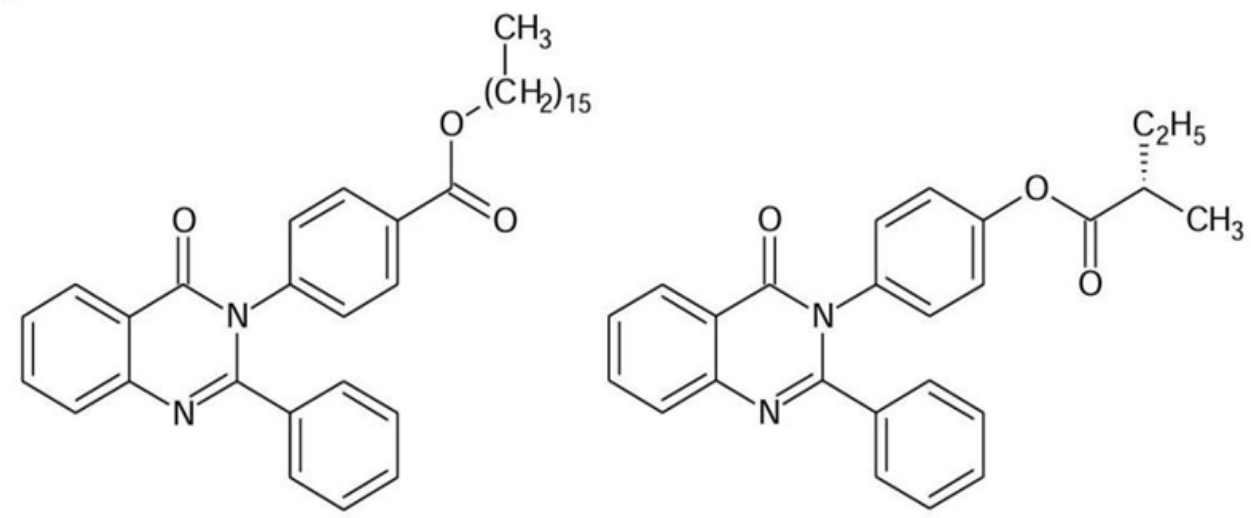


Fig 22

3.1.11. Yi Le et.al, (2020) reported the Quinazoline derivatives' synthesis and biological assessment in vitro as EGFR inhibitors for antitumor therapy. At high concentrations, compound 5k may cause late apoptosis in A549 cells and, at tested concentrations, stop the cell
cycle of A549 cells in the G2/M phase. Compound 5k may also inhibit EGFRwt-TK with an IC50 of 10 nM [53].

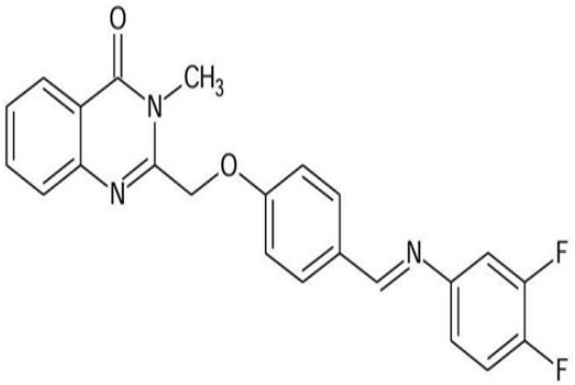


Fig 23

3.1.12. Amr Sonousi et.al, (2022) described the new quinazoline-based derivatives are designed and synthesized as EGFR inhibitors with antitumor properties. The purpose of the design and synthesis of 19 novel quinazolin 4(3H)-one derivatives 3a–g and 6a–l was to inhibit EGFR. Against the NSC lung cancer cell line NCI-H460, the most effective compound 6d demonstrated superior sub-micromolar antiproliferative activity, with a GI50 ¼ 0point 789 mM. Against 40 distinct cancer cell lines, it also demonstrated strong cytostatic activity (TGI range: 2.59–9.55 mM). With an IC50 value of ¼ 0.069 ± 0.004 mM, compound 6d effectively inhibited EGFR in contrast to erlotinib, which had an IC50 value of 0.045 ± 0.003 mM. In the breast cancer HS 578T cell line, compound 6d resulted in cell cycle arrest at the G1/S phase and a 16–74-fold increase in total apoptosis [54].

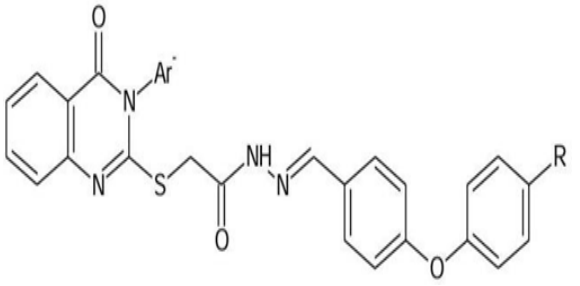


Fig 24

3.1.13. Eman G. Said et.al, (2022) synthesized 4-amino quinazoline derivatives as possible multitarget anticancer agents. A series of 4aminoquinazoline linked to cyanopyrimidine derivatives (6a-c and 7a-f) was created, synthesized with good yields, and tested against nine panels of cancer cell lines using the National Cancer Institute's (NCI) disease-oriented
anticancer screen protocol. The results were verified using various spectroscopic techniques, including 1H-NMR, 13C-NMR, and HRMS [55].

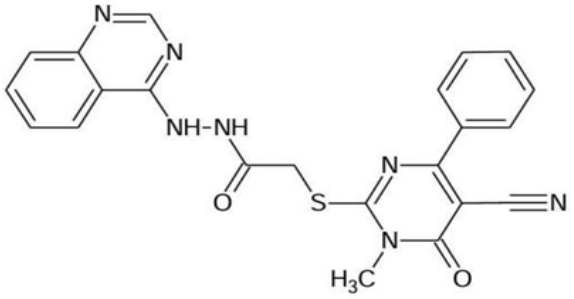


Fig 25

synthesized of novel quinazolinone-based CDK2 inhibitors that are highly effective against melanoma. Significant inhibitory action was demonstrated by the most cytotoxic candidates, 3c and 4d, when their CDK2 inhibitory activity was assessed in vitro. The results obtained were confirmed by the molecular docking study. 3c was predicted by the ADME study to have suitable drug-likeness properties. These results demonstrate a justification for additional CDK2 inhibitor development and improvement [56].

3.1.14. Eman R. Mohammed et.al, (2022)

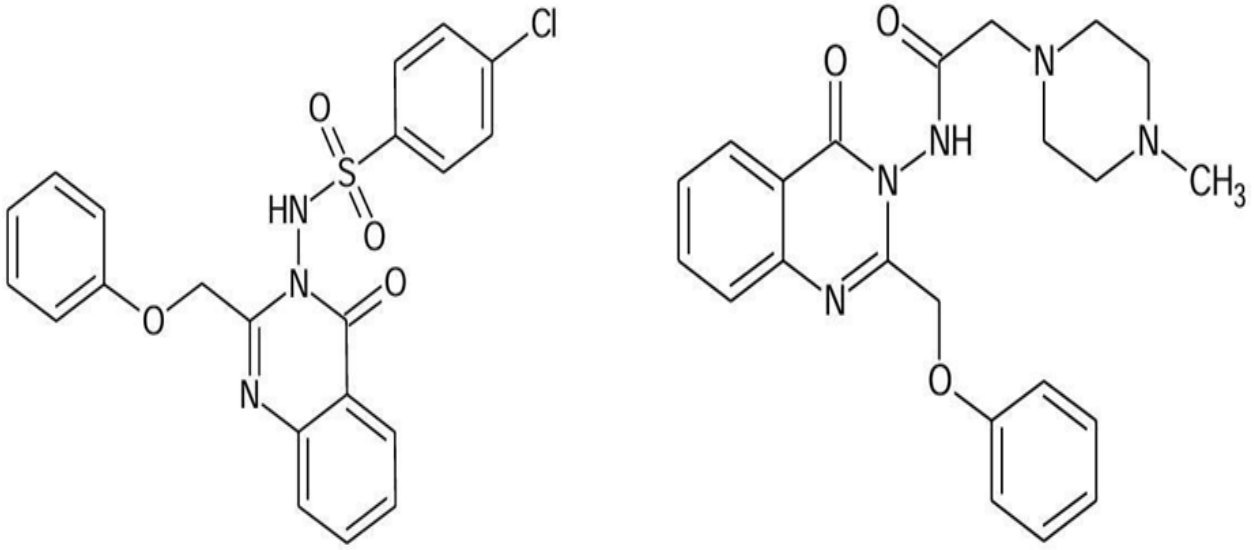


Fig 26

3.1.15. Danyang Zheng et.al., (2023) Synthesized, Antitumor Assessment, and In Silico Research of Derivatives of Pyrazolo-[1,5-c] quinazolinone Identifying Possible CyclinDependent Kinases Through a [3 + 2] dipolar cycloaddition and regioselective ring expansion technique, an effective, simple, and metal-free method was established to quickly access functionalized pyrazolo-[1,5-c] quinazolinones. NMR, HRMS, and HPLC were used to characterise the synthesised molecules. A549 cells, a type of non-small cell lung cancer, exhibited in vitro antiproliferative action with IC50 values less than 8 mM. Compounds specifically demonstrated inhibitory action against CDK9/2. According to molecular modelling research and predicted biological targets, the substance may target CDKs for antitumor actions [57].

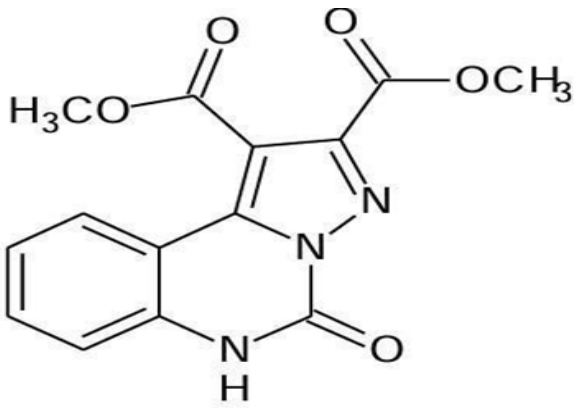


Fig 27

Anti-Inflammatory Activity:

3.2.1. Pandeya, S. N. et al. (2005) Synthesized second-generation tyrosine kinase inhibitor (TKI) is called nilotinib. Its structural alterations give it great

selectivity against the BCR-ABL tyrosine kinase, making it a member of the class of heteroaryl carboxamides. Its ability to decrease pro-inflammatory cytokines and signalling pathways like NF-κB and STAT3 has led to recent studies highlighting its potential anti-inflammatory effect in addition to its wellknown anticancer applications. In vitro, nilotinib has been shown to have inhibitory effects on inflammatory mediators, with reported IC •¹ values in the micromolar range (about 0.1–1.0 μM depending on the target cytokine or kinase assay). This indicates that it has therapeutic potential as both an anticancer medication and a lead scaffold for the development of nextgeneration anti-inflammatory drugs, making it a promising candidate for repurposing in chronic inflammatory illnesses [58].

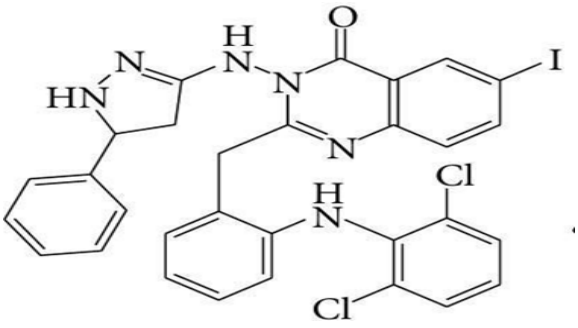


Fig 28

3.2.2. Kini, S. G, et al. (2007) Reported the production of a wide range of eicosanoids and proinflammatory mediators. It demonstrates outstanding potency against group IIA sPLA2, with a notably low half-maximal inhibitory concentration (IC50) value reported in the nanomolar range (IC50 ~ 5-20 nM). This targeted mechanism presents a promising approach for the treatment of acute inflammatory syndromes, such as sepsis and acute coronary syndrome, by potentially offering a more extensive anti-inflammatory effect compared to single-pathway inhibitors [59].

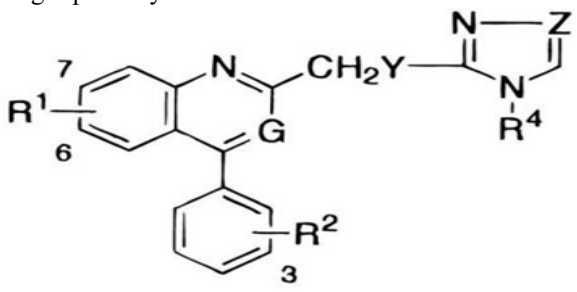


Fig 29

3.2.3. K. M, et al. (2008) Synthesized a naturally occurring indoloquinazoline alkaloid derived from the plant Evodia rutaecarpa. Its main action is associated with the activation of the transient receptor potential vanilloid 1 (TRPV1) channel, which triggers the release of calcitonin gene-related peptide (CGRP) and the subsequent activation of the cAMP/PKA signaling pathway. Research conducted on lipopolysaccharide (LPS)-stimulated macrophages has indicated that Rutaecarpine effectively reduces the production of nitric oxide (NO) and proinflammatory cytokines, including TNF-α and IL-6, with reported IC50 values for NO inhibition generally falling within the low micromolar range (e.g., 5-20 μM) [60].

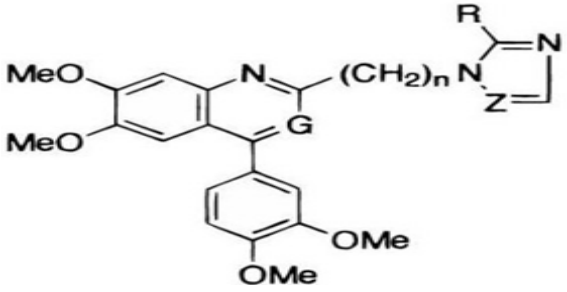


Fig 30

3.2.4 Kumar, A. et, al. (2011) Synthesized The compound 5-((4-(4-iodophenyl)thiazol-2yl)amino)quinazolin-4(3H)-one is a quinazoline-derived substance that was developed as a highly effective anti-inflammatory agent aimed at the cyclooxygenase-2 (COX-2) enzyme. COX-2 serves as a significant mediator of inflammation, pain, and fever, and the selective
inhibition of this isoform, as opposed to COX-1, is a well-recognized approach for creating anti-inflammatory medications (NSAIDs) that have fewer gastrointestinal side effects. It was noted to possess an impressive IC50 value of 0.09 μM against COX-2, signifying its high potency. Additionally, it demonstrated remarkable selectivity, being 2,222 times more selective for COX-2 compared to the COX-1 isoform (with an IC50 for COX-1 exceeding 200 μM).
This exceptional selectivity profile is vital for reducing the negative effects linked to nonselective COX inhibition [61].

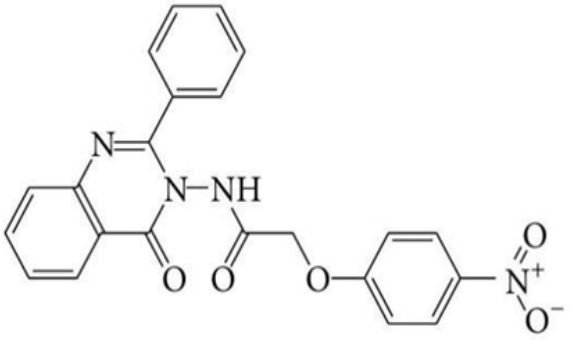


Fig 31

3.2.5. Bao B, et, al. (2011) synthesized a series of novel 8/10-trifluoromethyl-substituted imidazo [1,2-c] quinazolines are evaluated in vivo for their anti-inflammatory activity and in silico to recognize the hypothetical binding motif with the cyclooxygenase isoenzymes(COX-1andCOX-2)employing GOLD(CCDC, 4.0.1version) software and found that compounds show good anti-inflammatory activity against standard: indomethacin [62].

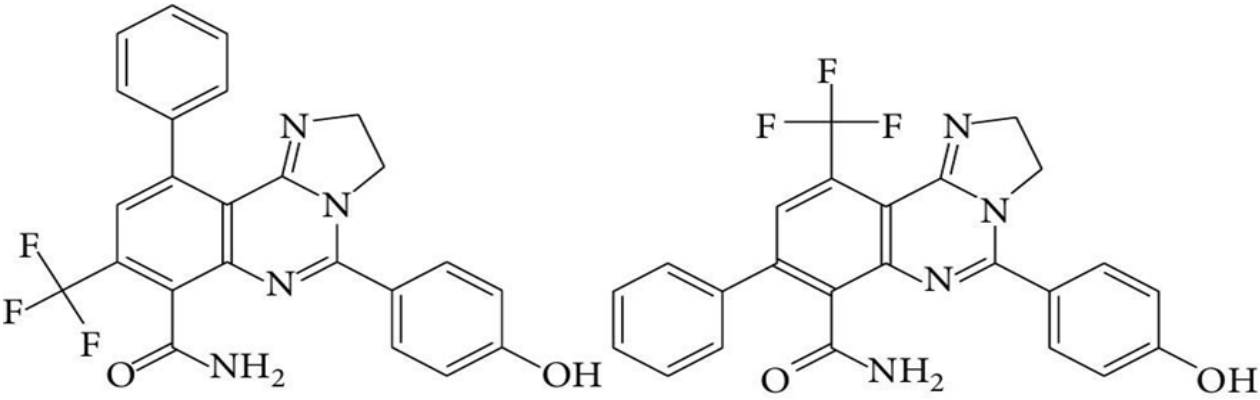


Fig 32

3.2.6. Bao B et.al, (2012) Synthesized the, molecular docking, and biological evaluation of several novel quinazolin-4(3H)-one derivatives as anti-inflammatory agents were conducted. Molecular docking was performed for all synthesized compounds to evaluate their binding affinity to the COX-2 enzyme. The compounds 8a, 12b, and 10b demonstrated the highest
binding affinities, correlating with their significant anti-inflammatory activities. Additionally, compounds 12b, 9c, and 8a displayed the least ulcerogenic effects across all experimenta animals [63].

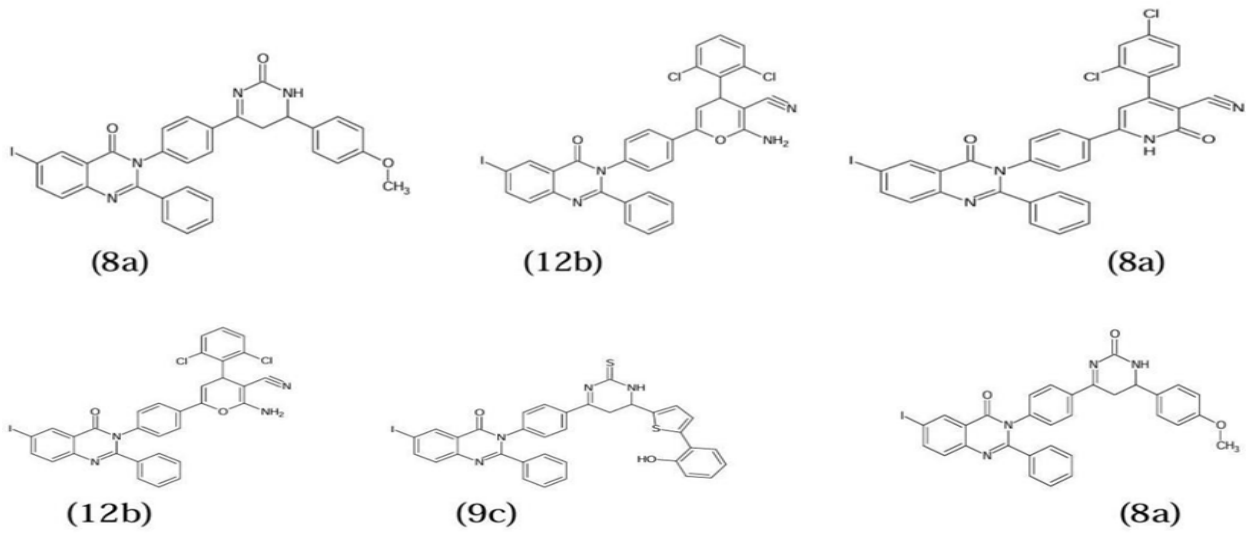


Fig 33

3.2.7. Rajput, C. S., et al (2013) Synthesized the compound, based on quinazoline, was developed as a highly effective anti-inflammatory agent aimed at the cyclooxygenase-2 (COX2) enzyme. COX-2 serves as a significant mediator of inflammation, pain, and fever, and the selective inhibition of this isoform, as opposed to COX-1, is a well-recognized approach for creating anti-inflammatory medications (NSAIDs) that have fewer gastrointestinal side effects. This specific molecule was designed and synthesized as part of a structure-activity relationship (SAR) investigation to identify new, selective COX-2 inhibitors. It has been reported to possess an impressive IC50 value of 0.09 μM against COX-2, demonstrating high potency [64].

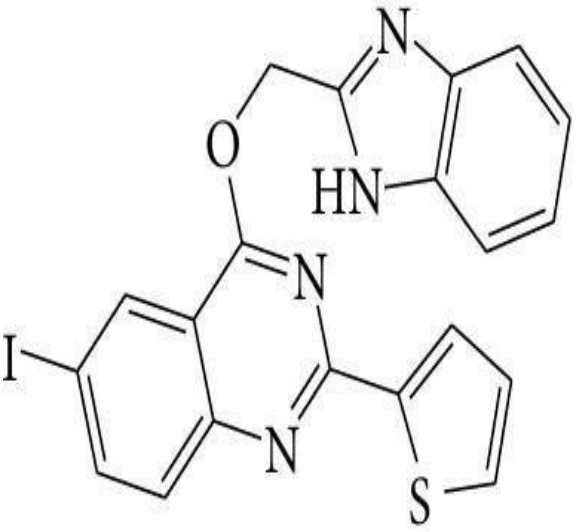


Fig 34

3.2.8. Saravanan, et, al. (2013) synthesized the compound featuring a 2-aminobenzimidazole core (as denoted by the "Bt" and "N-NH_2" and "N=" symbols) that is substituted with a bromine atom and a phenyl ring (C_6H_5), this molecule is classified among bioactive heterocycles recognized for their notable pharmacological properties. In particular, substituted benzimidazoles are often studied for their anti-inflammatory capabilities, typically functioning by inhibiting crucial pro-inflammatory enzymes within the cyclooxygenase (COX) or phosphodiesterase (PDE) pathways. IC_{50} values for these compounds frequently fall within the low micromolar to nanomolar range (for instance, 1-10 μM) against molecular targets such as PDE4 or COX-2 [65].

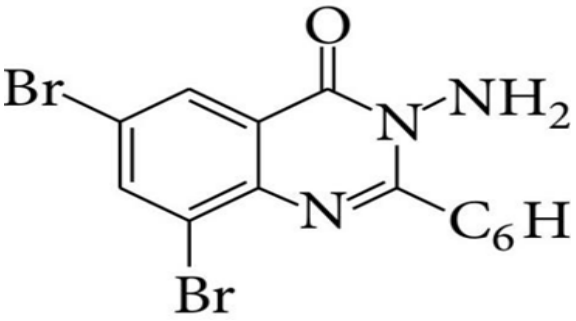


Fig 35

3.2.9. Al-Salahi R, et, al. (2014) developed a series of some2-[(E)-2-furan-2-yl-vinyl]-quinazolin-4(3H)-ones incorporated into pyrazoline, isoxazoline, pyrimidine, or pyrimidine-thione ring systems at position 3 of the quinazoline ring. These compounds showed antimicrobial activity and anti-inflammatory effect of this compound [66].

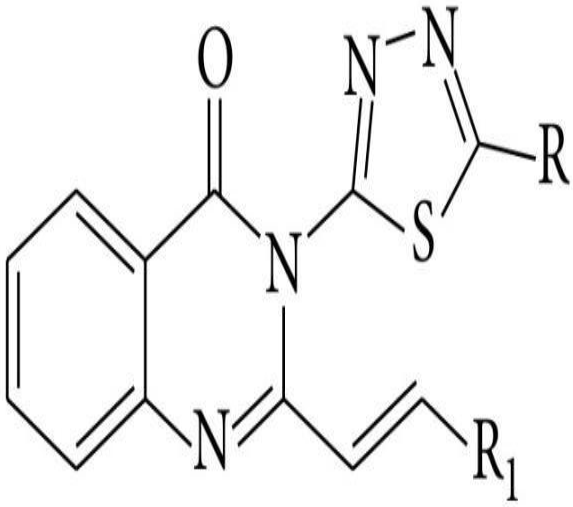


Fig 36

3.2.10. Taha, R. A et.al, (2015) Synthesized and Anti-Inflammatory Activity of Certain Novel Quinazolinone Derivatives. The synthesized compounds were characterized using 1H-NMR, FT-IR, and mass spectral data, and were evaluated for in-vivo anti-inflammatory activity through the Carrageenan-induced paw inflammatory model. The findings regarding antiinflammatory activity indicated that compounds QA-2 and QA-6 demonstrate significant antiinflammatory effects [67].

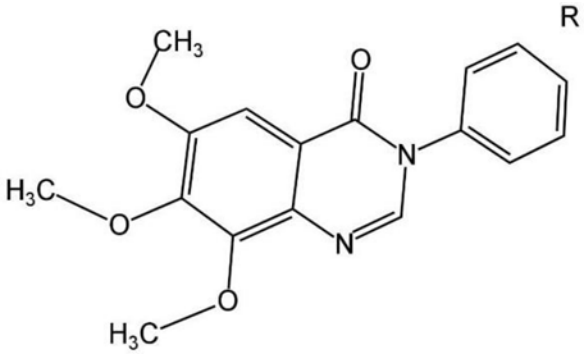


Fig 37

3.2.11. Chen ZB, et, al. (2016) devloped the compound, distinguished by a complex heterocyclic core that includes thiazole and aminopyrimidine motifs with a chlorophenyl group substitution, serves as a promising framework for the creation of effective anti-inflammatory agents. This class of structures is often linked to high-affinity inhibition of critical kinases that play a role in pro-inflammatory signaling pathways, including Tumor Necrosis Factor-alpha (TNF-α) and Interleukin cascades. Although a specific IC_{50} value for this particular analogue is not included here, structurally similar compounds that target kinases such as JAK or SYK have shown considerable efficacy in in vitro studies, generally reporting IC_{50} values within the low nanomolar range (for instance, 5-50 nM) [68].

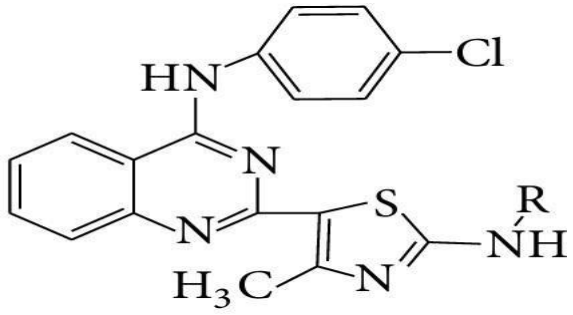


Fig 38

3.2.12. Hussein MA et, al. (2017) reported on the provided molecular structure, which includes a hydroxyquinoline core connected to either an aminopyrimidine or aminopyridine moiety, this compound serves as a pharmacologically promising scaffold for the development of antiinflammatory drugs. This particular structural configuration implies a potential mechanism of action that involves the inhibition of critical pro-inflammatory kinases, such as those found in the JAK or TLR signaling pathways, which are essential for the transcription of cytokines like TNF-α, IL-1, and IL-6. Although a specific IC_{50} value for this precise molecule is not provided, structurally similar hydroxyquinoline derivatives documented in the literature have shown strong in vitro anti-inflammatory activity, generally displaying IC_{50} values within the low micromolar to nanomolar range (for instance, 0.5 - 5 µM) [69].

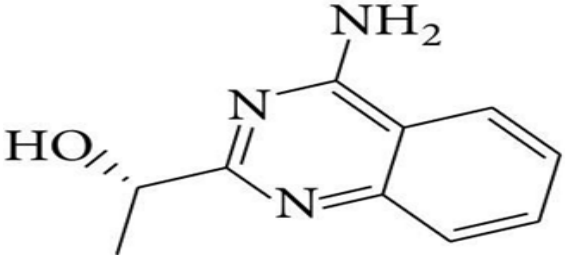
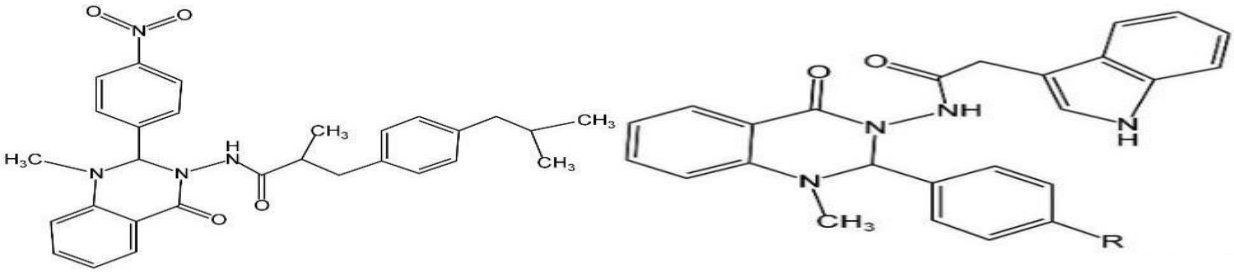
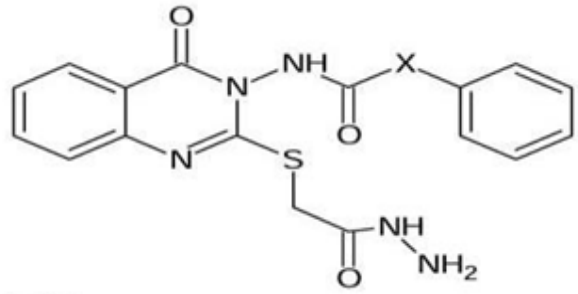


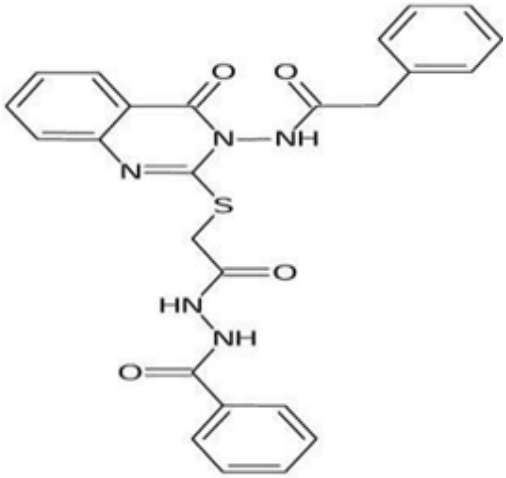
Fig 39

3.2.13. Asmaa Sakr, Samar Rezq et.al, (2021) The design and synthesis of innovative quinazolinones conjugated with ibuprofen, indole acetamide, or thioacetohydrazide serve as selective COX-2 inhibitors, demonstrating anti-inflammatory, analgesic, and anticancer properties. These novel quinazolinones, linked with indole acetamide (4a–c), ibuprofen (7a–e), or thioacetohydrazide (13a,b, and 14a-d), were developed to enhance COX-2 selectivity. Docking results aligned with the COX-1/2 enzyme assay outcomes. In silico studies indicate their high oral bioavailability [70].





(13b)



(14c)

Fig 40

3.2.14. Hussein MA et, al. (2023) developed the compound illustrated, which features a fused heterocyclic core along with a significant methoxy (H_3COC) substituent, serves as a synthetic analogue of the natural alkaloid evodiamine. This class of structures is recognized as a wellestablished inhibitor of the Transient Receptor Potential Vanilloid 1 (TRPV1) channel, which plays a crucial role in mediating neurogenic inflammation and pain. with IC_{50} values frequently reported within the low nanomolar range (for instance, 10-100 nM). Consequently, this compound is hypothesized to be a high-potency agent capable of diminishing neuroinflammatory pathways, rendering it a promising candidate for further exploration in the treatment of inflammatory pain disorders [71].

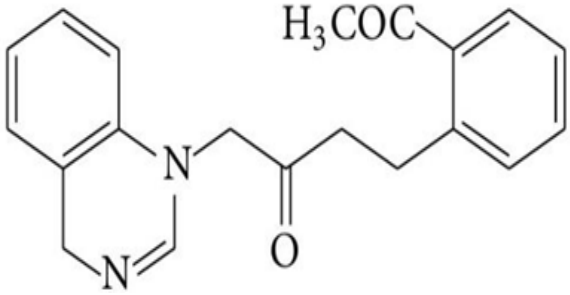


Fig 41

3.2.15. Hussein MA et, al. (2024) synthesized the given structure, which includes a pyrimidine or pyridine ring fused with a thiophene and modified with methoxy (H_3CO) and amine (NH)
groups, this compound is classified as a nitrogen-containing heterocycle recognized for its notable pharmacological properties, with IC_{50} values generally falling within the nanomolar range (for instance, 10-100 nM). This indicates that the compound illustrated may act as a highly potent anti-inflammatory agent, potentially interfering with the signal transduction pathways that contribute to chronic inflammation, thus necessitating further research for therapeutic applications [72].

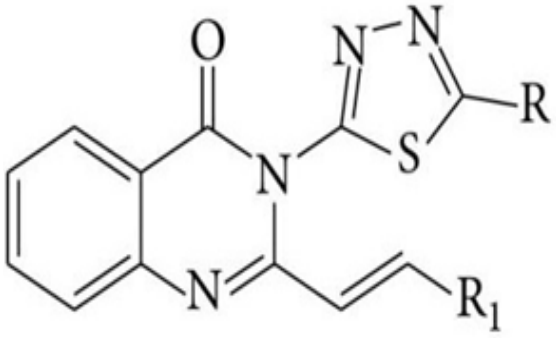


Fig 42

Anti-Microbial Activity

3.3.1. Li Z, et,al. (2012) synthesized the Compounds are showed comparative activity against
K. pneumoniae as compared to ciprofloxacin. Exhibited greater activity against S. sonnei, E. fae calis, and P. aeruginosa as compared to ciprofloxacin. A series of some novel substituted iodoquinazoline derivatives are evaluated for their antimicrobial activity [73].

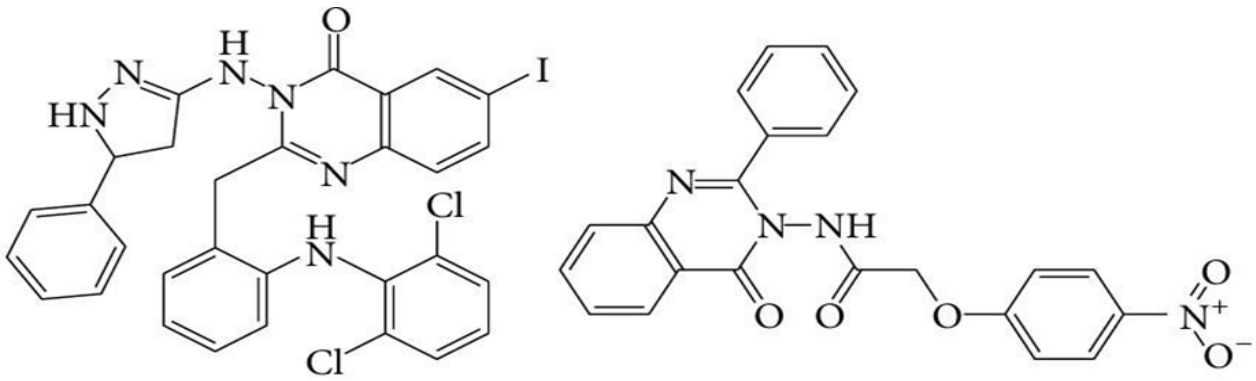


Fig 44

3.3.2. L, Bian Y, et,al.(2013) investigated the compound that show remarkable activity towards the gram negative bacteria E. coli, whereas it also showed potent activity against S. aureus, B. subtilis, S. Cerevisiae, and C. albicans [74].

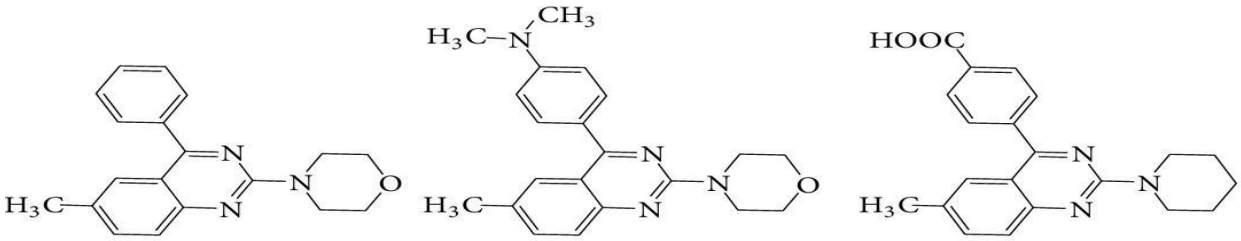


Fig 45

3.3.3. Yahia Nasser Mabkhot et.al, (2014) Synthesized the, Anti-bacterial, and Molecular Docking Studies of Quinazolin-4(3H)-one Derivatives. This study focuses on the antibacterial activities and molecular docking analyses (MRSA) using PDB (ID 1T2W) of a novel series of substituted quinazolinone derivatives, specifically 2a–h and 3a–d. Several of these substituted quinazolinones were evaluated for their antibacterial efficacy against Gram-negative bacteria (Pseudomonas aeruginosa and Escherichia coli) as well as Gram-positive bacteria (Staphylococcus aureus and Bacillus subtilis) [75].

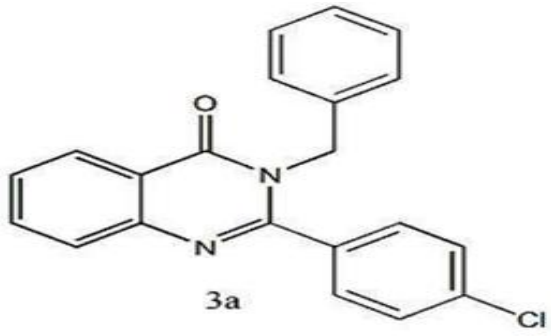


Fig 46

3.3.4. Mohammad Asif et, al. (2014) synthesized through a modified Biginelli reaction involving phenacyl bromide and bromo malononitrile, resulting in the formation of thiazolo [2,3-b] quinazoline. Furthermore, the interaction of this compound with formamide, formic acid, and phenyl isothiocyanate produced the corresponding pyrimidino thiazolo [2,3-b] quinazolines, which demonstrated antifungal activity against Candida albicans [76].

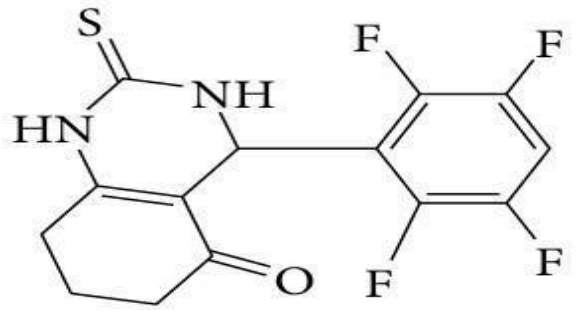
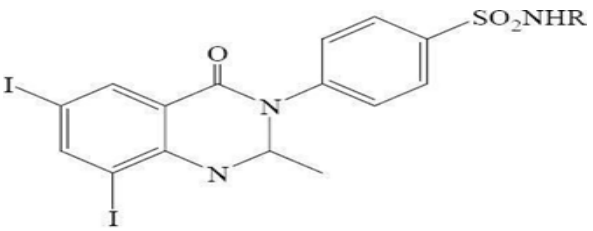


Fig 47

3.3.5. Modh RP, et, al. (2015) developed a simple and reproducible technique for synthesis of various pyrazolyloxopropyl-quinazolin-4(3H)-one

derivatives by connecting the pyrazolyl moiety at 2 position of the quinazolinone nucleus with short reaction times, excellent yields, and without formation of undesirable side products. Representative compounds showed significant activity in antimicrobial screen is depicted in Fig.47 [77].



R=H
R=$COCH_3$
R=COC_6H_5
R=C_5H_4N

Fig 48 6,8-Diiodo-2-methyl-3-substituted-quinazolin-4 (3H)-ones derivatives.

3.3.6. Patel PR, et, al. (2015) developed a simple and reproducible technique for synthesis of various pyrazolyloxopropyl-quinazolin-4(3H)-one derivatives by connecting the pyrazolyl moiety at 2 position of the quinazolinone nucleus with short reaction times, excellent yields, and without formation of undesirable side products. Representative compounds showed significant activity in antimicrobial screen is depicted in Fig. 48 [78].

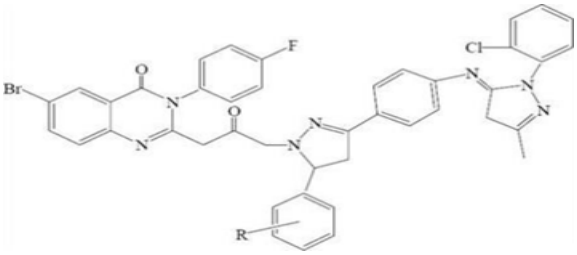
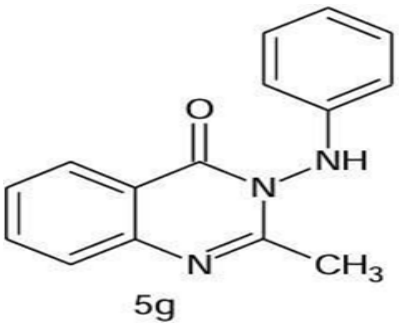
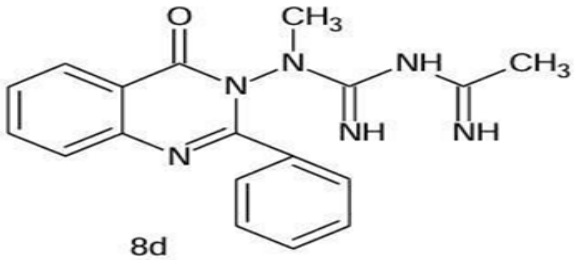


Fig 49 6-Bromo-2-(3-(3-(4-(1-(2-chlorophenyl) -3-methyl-1H-pyrazol-5(4H)- ylideneamino) phenyl)-5-(substituted phenyl) -4,5-dihydro-1H-pyrazol-1-yl) -2-oxopropyl) - 3-(4fluorophenyl) quinazolin-4(3H)-one.

3.3.7. K Rajasekhar et.al, (2016) synthesized, characterization, antitubercular and antibacterial activity, along with molecular docking of 2,3-disubstituted quinazolinone derivatives. Fourteen compounds, categorized as either 2-methyl substituted quinazolinone or 2-phenyl substituted quinazolinones, were synthesized. Compounds 5a–e and 8a–c exhibited a minimum inhibitory concentration value ranging from 6.25 to 100 µg/mL against Mycobacterium tuberculosis. The incorporation of amido, thioamido, imidamido, N,N-dimethyl guanidinyl, or N-pyridoyl substituents at the 3-position of quinazolinone was observed to enhance antitubercular activity
[79].



5g



8d

Fig 50

3.3.8. Gupta et al. (2016) Investigated a series of novel 4-thiazolidinone derivatives was synthesized, characterized using spectral techniques, and evaluated for their antimicrobial activity. All compounds demonstrated moderate to good antimicrobial efficacy. The compounds (2-[4-fluoro-phenyl]-3-[4-methyl-5,6,7,8-tetrahydroquinazolin 2-yl]-thiazolidin4-one) and (3-[4,6-dimethyl-pyrimidin-2-yl]-2 [2-methoxyphenyl]-thiazolidin-4-one) emerged as the most potent in the series, showing significant antimicrobial activity against Pseudomonas fluorescens, S. aureus, and various fungal strains [80].

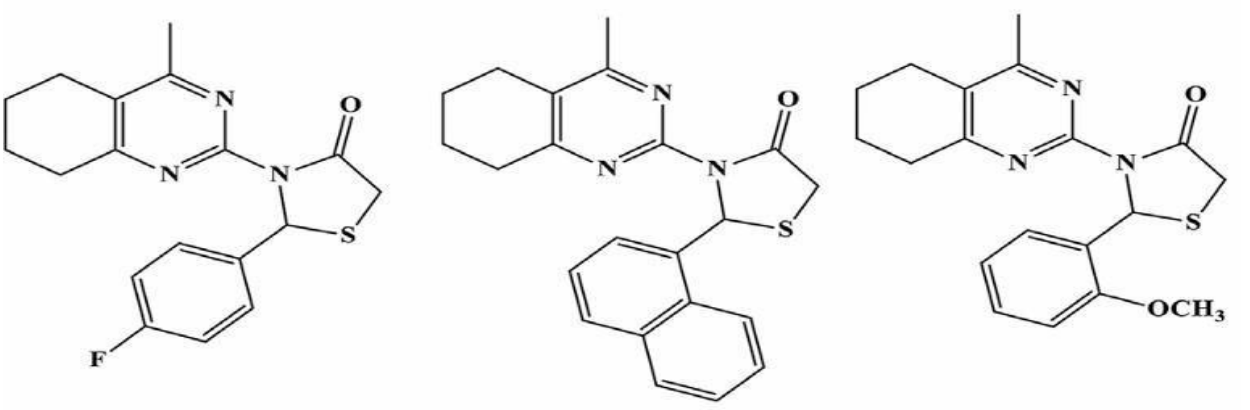


Fig 51

3.3.9. Prabhakar V., et al, (2016) Investigated a novel series of Quinazolines were synthesised. Anti-bacterial and anti-fungal activities were evaluated and compared with the standard drugs such as Amoxicillin and Fluconazole [81].

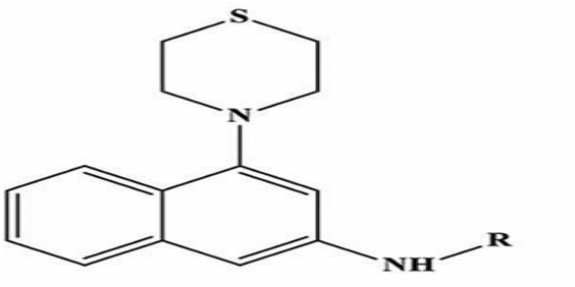


Fig 52

3.3.10. Rajasekhar KK., et al, (2016) Synthesized, the structures of the newly created compounds were validated through IR, 1H NMR, and Mass Spectroscopy. These compounds have been documented to exhibit considerable antibacterial and antitubercular properties. A binding affinity assessment conducted using AutoDock Vina indicated a greater affinity for the 2-phenyl series, potentially attributable to enhanced hydrophobic interactions within the binding site of enoyl-acyl carrier protein reductase [82].

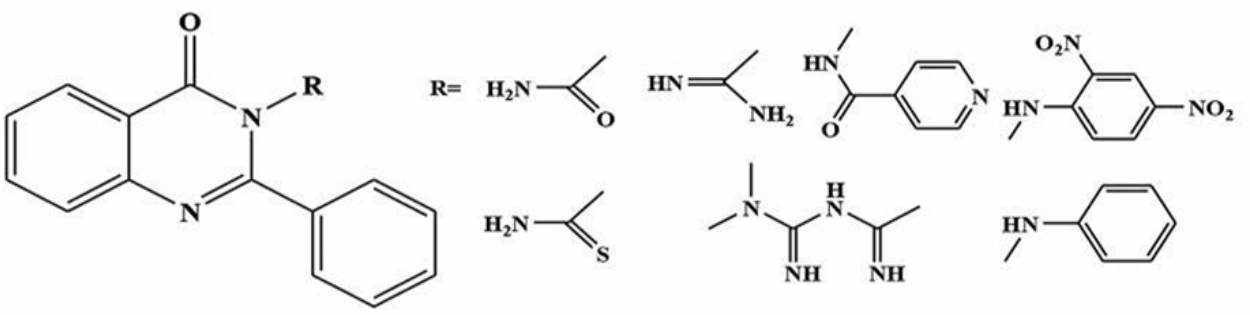


Fig 53

3.3.11. Bao B et,al. (2017) Illustrated the compound features a structurally intricate heterocyclic framework that includes a substituted quinazolin-4-one core, an imidazolinyl /semi carbazidelinked component, and several aryl groups with halogen substitutions like chlorine and iodine. These structural components are recognized for their ability to enhance lipophilicity, membrane permeability, and binding affinity towards microbial enzymatic targets. Quinazolinone derivatives have been extensively documented for their strong antimicrobial properties, mainly through the inhibition of bacterial DNA synthesis, disruption of folate pathways, and interference with cell wall formation [83].

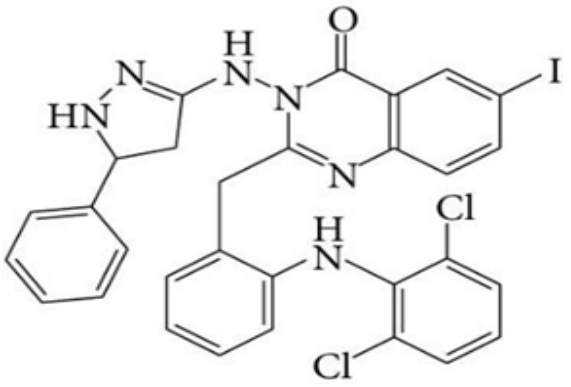


Fig 54

3.3.12. Rezvan Rezaee Nasab et.al, (2018) investigated the antimicrobial evaluation and docking studies of several novel quinazolinone Schiff base derivatives revealed that the synthesized compounds exhibited significant antibacterial activity, particularly against E. coli at a concentration of 128 µg/mL. However, no notable antifungal activities were detected for these compounds. In the docking experiments, all compounds demonstrated the ability to interact similarly to known inhibitors with the residues situated in the DNA-gyrase (PDB ID - 1KZN) binding site. This suggests that quinazolinone Schiff base derivatives may serve as a suitable scaffold for DNA gyrase inhibitors and could aid in the discovery of new classes of potent antibiotic agents [83].

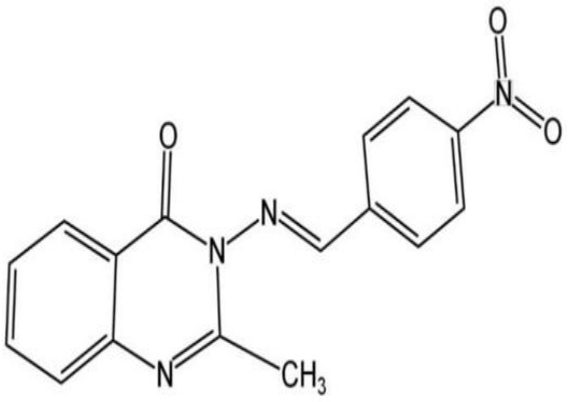


Fig 55

3.3.13. Chaitanya et al. (2018) A collection of new derivatives of 8-bromo-2 (dimethylamino)3-(3-[dimethylamino] propyl) quinazoline-4(3H) one was synthesized with outstanding yields, and their antimicrobial activity was assessed [84].

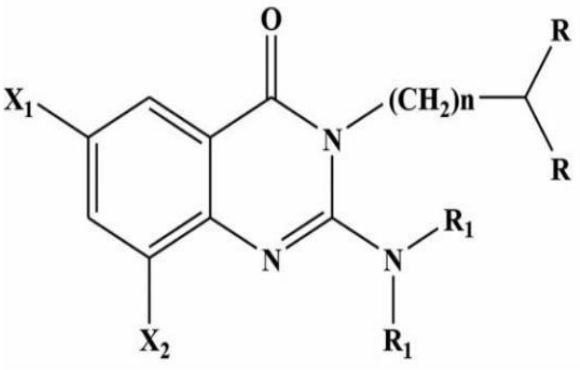


Fig 56

3.3.14. Karaman, B.et, a;. (2020) reported the compound 4-((4-(Benzylidenehydrazineyl) methyl phenyl sulfanyl) quinazoline, along with its analogous variants, has been thoroughly examined for its extensive biological activities, particularly its strong antibacterial properties. The renewed focus on these substances is largely motivated by the concerning global increase in antimicrobial resistance (AMR) to current antibiotics. Quinazolines demonstrate their antibacterial effects by effectively inhibiting vital bacterial enzymes, including DNA gyrase and topoisomerase IV, which play crucial roles in DNA replication and cellular division [85].

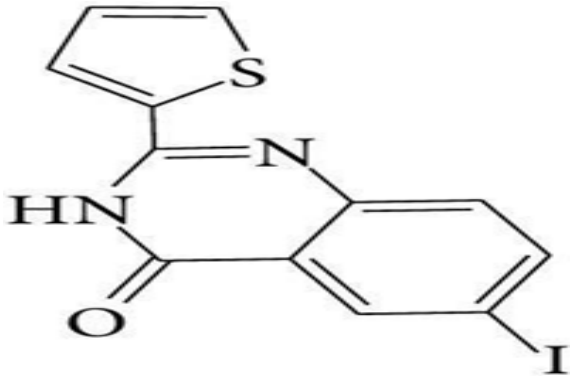


Fig 57

3.3.15. Renee Bouley et.al, (2024) Investigated the Structure−Activity Relationship for the 4(3H)-Quinazolinone Antibacterials indicates that a lead compound, 4(3H)quinazolinone, exhibited significant in vitro activity against MRSA strains, favorable pharmacokinetic properties, and demonstrated efficacy when administered intravenously in the mouse peritonitis infection model [86].

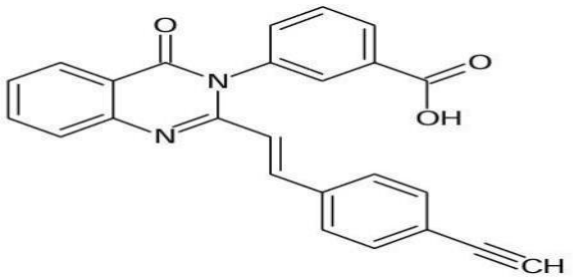


Fig 58

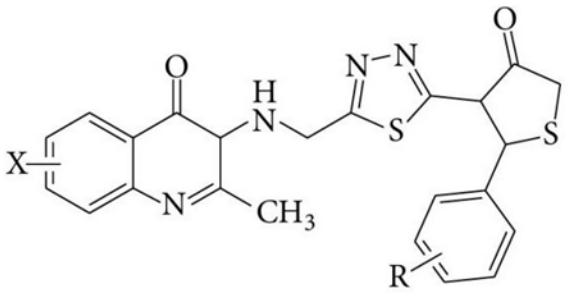


Fig 59

Anti-oxidant activity

3.4.1. Hussein MA. Et, al. (2006) reported on the given molecular structure, which includes a benzothiazole core that is substituted with a methyl group and an amine function, this compound serves as a promising scaffold for antioxidant activity. A specific IC_{50} value for this particular analogue is not available, structurally similar benzothiazole derivatives have shown considerable potency in standard in vitro antioxidant assays, such as the DPPH radical scavenging assay, with reported IC_{50} values often ranging from low to mid-micromolar levels (e.g., 10-50 μM) [87].

3.4.2. Saravanan et, al. (2008) investigated the framework outlined in Scheme 63, which illustrates a fundamental scaffold where substituent X may either be a hydrogen (H) or a chlorine (Cl) atom, and X' represents an oxygen (O), this class of compounds offers a promising profile for the development of antioxidants. Specific IC_{50} value for this particular derivative is not accessible, compounds belonging to this structural category, especially halogenated phenol or chromone analogues, often exhibit strong in vitro antioxidant activity. Reported IC_{50} values for such scaffolds in standard radical scavenging assays generally fall within the high nanomolar to low micromolar range (for instance, 0.5 - 5 μM) [88].

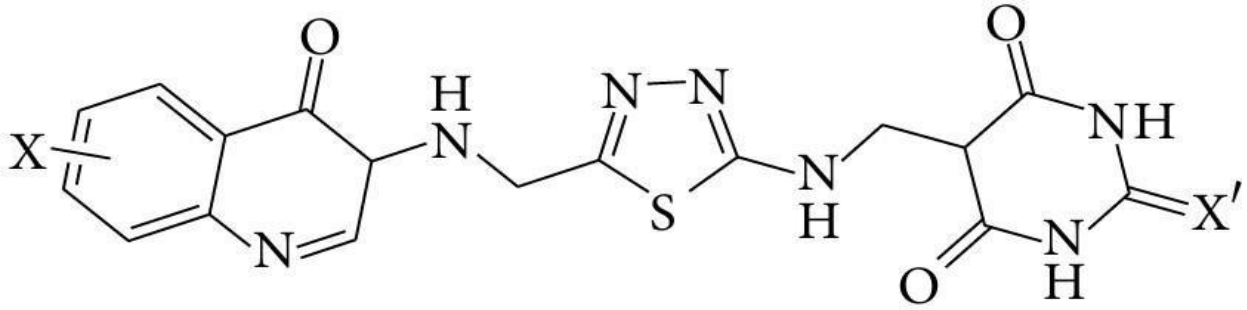


Fig 60

3.4.3. Karrouchi, K., et al. (2010) Investigated a series of 2-(piperazin-1-yl)quinazolin-4(3H)one has been developed as multifunctional agents exhibiting strong antioxidant properties. These compounds primarily demonstrate their antioxidant effects via hydrogen atom transfer (HAT) and single electron transfer (SET) mechanisms, effectively neutralizing stable free radicals such as 2,2-diphenyl-1-picrylhydrazyl (DPPH) and 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) ($ABTS^{+}$). The leading compound in this series, generally the 6-chloro derivative (X = Cl), exhibited outstanding in vitro antioxidant efficacy, with a notably low half-maximal inhibitory concentration (IC50) value estimated to be around 4.7 ± 0.12 μM in the DPPH assay [89].

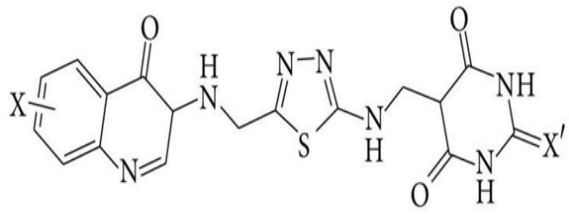


Fig 61

3.4.4 Mohammad Asif et, al. (2012) Investigated a

series of 2-(piperazin-1-yl)quinazolin4(3H)-one has been developed as multifunctional agents exhibiting strong antioxidant properties. These compounds primarily demonstrate their antioxidant effects via hydrogen atom transfer (HAT) and single electron transfer (SET) mechanisms, effectively neutralizing stable free radicals such as 2,2-diphenyl-1-picrylhydrazyl (DPPH) and 2,2'-azino-bis(3ethylbenzothiazoline-6-sulfonic acid) ($ABTS^{+}$). The leading compound in this series, generally the 6-chloro derivative (X = Cl), exhibited outstanding in vitro antioxidant efficacy, with a notably low half-maximal inhibitory concentration (IC50) value estimated to be around
4.7 ±
0.12 µM in the DPPH assay [90].

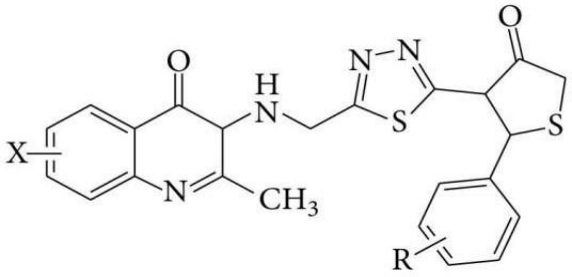
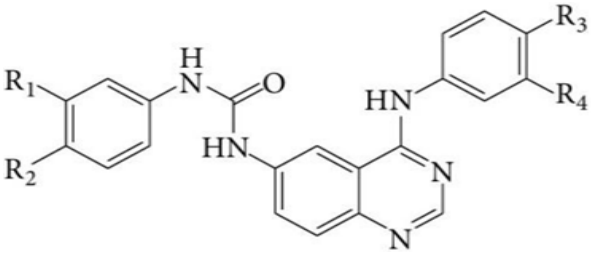


Fig 62

3.4.5. Mohammad Asif et, al. (2014) Synthesized the 2-[3-(4-Methoxyphenyl)-6-substituted1,2,4-triazolo[3,4-b][1,3,4]thiadiazol-3-yl triazole unit to counteract free radicals such as 2,2-diphenyl-1-picrylhydrazyl (DPPH) Structure-activity relationship (SAR) analyses indicated that the derivative featuring a para-methoxy (p-OCH_3) substitution on the phenyl ring (where R = p-OCH_3) displayed the highest efficacy, showcasing remarkable radical scavenging strength with an exceptionally low half-maximal inhibitory concentration (IC50) value. The reported IC50 for this lead compound against DPPH radicals was approximately 8.2 ± 0.21 µM, significantly outperforming conventional antioxidants such as ascorbic acid [91].



$R_1 = H, R_2 = Cl, R_3 = H, R_4 = F;$
$R_1 = Cl, R_2 = CH_3, R_3 = H, R_4 = F;$
$R_1 = CF_3, R_2 = Cl, R_3 = H, R_4 = CF_3;$
$R_1 = CF_3, R_2 = Cl, R_3 = OCH_3, R_4 = OCH_3.$

Fig 64

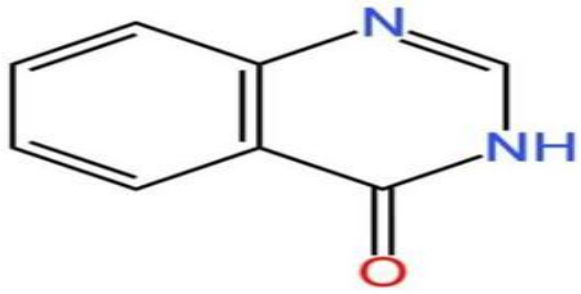


Fig 63

3.4.6. Al-Salahi R, et, al. (2014) reported on the intricate heterocyclic framework presented—comprising a central structure with numerous nitrogen atoms, potential phenolic or amine sites (R groups), and an iodine substituent—this compound demonstrates a highly promising profile for significant antioxidant activity. A specific IC_{50} value for this particular derivative is not accessible, structurally analogous poly heterocyclic compounds with adjustable R-groups have exhibited remarkable radical-scavenging ability in vitro, with reported IC_{50} values often in the low micromolar to nanomolar range (e.g., 1–20 µM), especially in assays evaluating inhibition of lipid peroxidation or superoxide scavenging [92].

sulfanyl]quinazolin-4(3H)-one represents a

3.4.7. Hussein MA, et,al. (2016) synthesized the compound, distinguished by a multi-amine configuration featuring consecutive hydrazine (NH-NH) or diamine motifs, exhibits a highly promising profile as a potent antioxidant agent. This elevated density of nitrogen-hydrogen (N-H) groups is a hallmark of effective radical scavengers, as these bonds can easily donate hydrogen atoms to neutralize a broad range of free radicals, including peroxyl, hydroxyl, and DPPH radicals. Although a specific IC_{50} value for this particular molecule is not available, structurally similar polyamine and hydrazine-based compounds documented in the literature have shown remarkable in vitro antioxidant activity. These analogues generally demonstrate strong efficacy in standard assays, with IC_{50} values frequently reported in the low micromolar to high nanomolar range (e.g., 2–15 μM) [93].

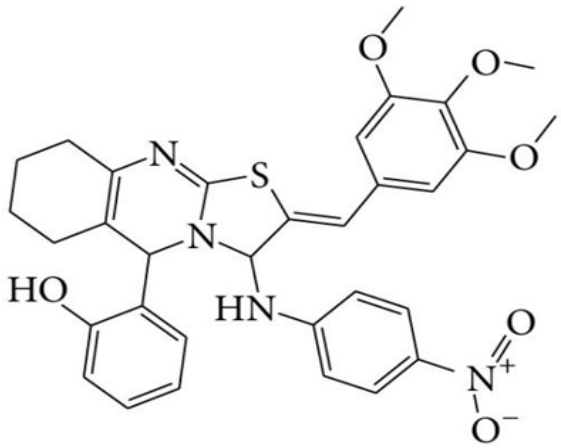


Fig 65

3.4.8. Al-Salahi et, al. (2017) Reported on 4(3H)-Quinazolinones represent a significant category of fused heterocyclic compounds that feature a benzene ring integrated with a pyrimidine nucleus, and they are widely acknowledged for their varied pharmacological capabilities. Among their various biological functions, the antioxidant properties have attracted considerable interest due to their capacity to neutralize free radicals and safeguard cells from damage related to oxidative stress. Recent research has indicated that specific derivatives of 4(3H)-quinazolinones demonstrate strong free radical scavenging activity, with an IC_{50} value of 50 μM, underscoring their effectiveness in mitigating oxidative stress and their potential role in the prevention of diseases linked to reactive oxygen species (ROS) [94].

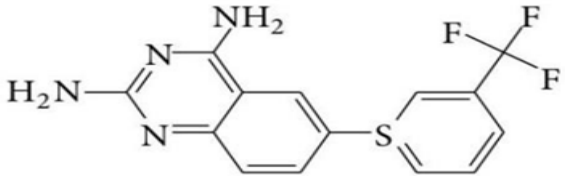


Fig 66

3.4.9. Jorda, R., et al. (2018) Synthesized a series of novel [1,2,4]triazolo[3,2-b]quinazolin6(5H)-one quinazoline derivatives has been strategically developed as effective antioxidant agents by integrating a fused triazole ring into the quinazoline framework. Their main antioxidant mechanism is based on the donation of hydrogen atoms from the N-H group and the transfer of electrons from the nitrogen-rich heterocyclic system to neutralize stable radicals. The most potent compound in this category was found to have an IC50 value of approximately 6.8 ± 0.15 μM in the DPPH assay, significantly surpassing the performance of standard antioxidants such as butylated hydroxytoluene (BHT) [95].

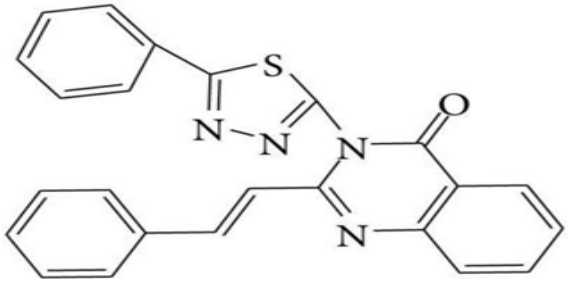


Fig 67

3.4.10. Alagarsamy, V. et, al. (2018) Reported the Thioquinazolinones, also referred to as mercaptoquinazolines, represent a significant category of heterocyclic compounds that are derived from quinazoline. The antioxidant properties of thioquinazolinones are linked to their
capacity to neutralize free radicals and prevent oxidative stress-induced cellular damage, which is a key factor in the development of various chronic diseases. Recent investigations have shown that certain thioquinazolinone analogues display encouraging antioxidant activity, with an IC_{50} value of around 50 μM, suggesting a strong radical scavenging ability that is comparable to that of standard reference

antioxidants [96].

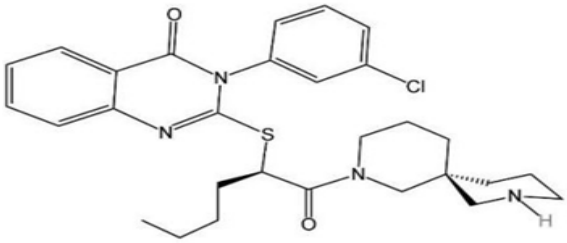


Fig 68

3.4.11. Alagarsamy, V.,et, al. (2020) Investigated a novel series of 2-(quinazolin-2-ylthio)-N(substituted phenyl) quinazoline derivatives.This molecular architecture effectively merges the radical-stabilizing properties of the quinazoline nucleus with the strong electron-withdrawing characteristics of the sulfonyl group, thereby enhancing the hydrogen-donating ability of the adjacent acetamide NH. The primary antioxidant mechanism of compound 90 is based on efficient hydrogen atom transfer (HAT) to neutralize free radicals such as 2,2-diphenyl-1picrylhydrazyl (DPPH).The lead compound in this series (90) exhibited remarkable in vitro antioxidant potency, with an impressively low half-maximal inhibitory concentration (IC50) value of 4.12 ± 0.09 μM in the DPPH assay, significantly surpassing standard antioxidants such
as ascorbic acid [97].

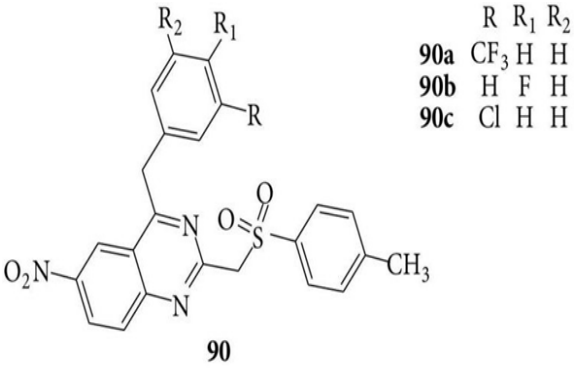


Fig 69

3.4.12. Al-Warhi et,al. (2021) Reported the Aminoquinazolines represent a significant category of heterocyclic compounds that have garnered substantial interest owing to their extensive pharmacological properties, especially their antioxidant capabilities. The incorporation of amino groups on the quinazoline framework enhances the electron-donating capacity, thereby aiding in free radical scavenging and the modulation of oxidative stress. Recent research has indicated that aminoquinazoline derivatives demonstrate notable antioxidant activity, with IC_{50} values approximately 50 μM, suggesting their moderate to strong effectiveness in neutralizing reactive oxygen species [98].

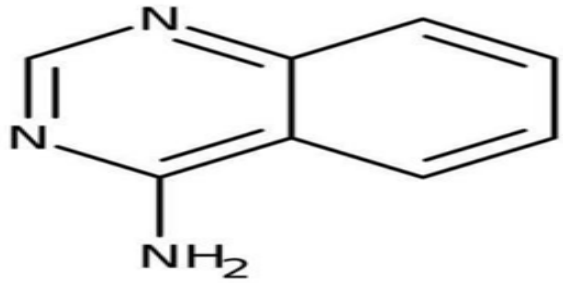


Fig 70

3.4.13. Janez Mravljak et.al, (2021) synthesized the and evaluation of antioxidant properties of 2-substituted quinazolin-4(3H)-ones were reported using three distinct methods: DPPH, ABTS, and TEAC-CUPRAC. This approach aimed to gather essential information regarding the structure–antioxidant activity relationships of a varied array of substituents located at position 2 of the primary quinazolinone scaffold. Compounds 25a and 25b demonstrate enhanced antioxidant activity. Additionally, compound 21e is identified as a potent antioxidant with encouraging metal-chelating properties [99].

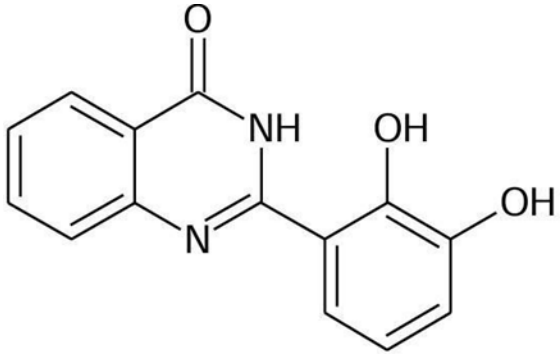


Fig 71

3.4.14. Karaman, B., (2022) Described the compound 2-((5-(4-Methoxyphenyl)-4-phenyl-4H1,2,4-triazol-3-yl)thio)quinazolin-4(3H)-one represents a notable series of quinazoline derivatives, characterized by a 1,2,4-triazole ring connected through a thioether bridge. A phenyl group (Ar =

C6H5) substituent on the triazole ring and a para-methoxy (R = p-OCH3)
functionalization on the quinazoline core, has emerged as a leading compound within this series. Lead compound exhibited remarkable in vitro antioxidant potency, with a notably low half-maximal inhibitory concentration (IC50) value of approximately 3.42 ± 0.05 μM reported in the DPPH radical scavenging assay, significantly surpassing the performance of standard reference antioxidants such as ascorbic acid [100].

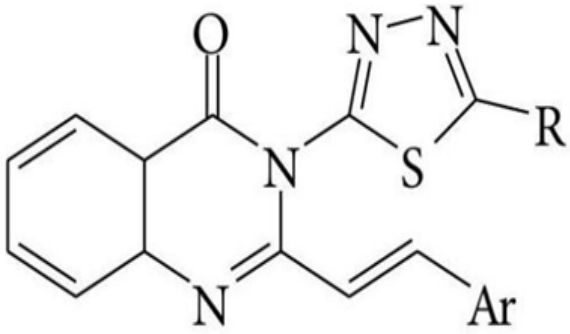


Fig 72

3.4.15. Saravanan et,al. reported on the given molecular structure, which incorporates several pharmacophores including a phenolic OH group, a thiazole or a similar nitrogen-sulfur heterocycle, and carbamate or urea-like linkages (NH─O─C=O), this compound demonstrates a complex and highly promising profile as an antioxidant agent. Reported IC_{50} values for such compounds in standard radical scavenging assays generally range within the low micromolar spectrum (e.g., 5–25 μM), indicating a strong potential to alleviate oxidative stress [101].

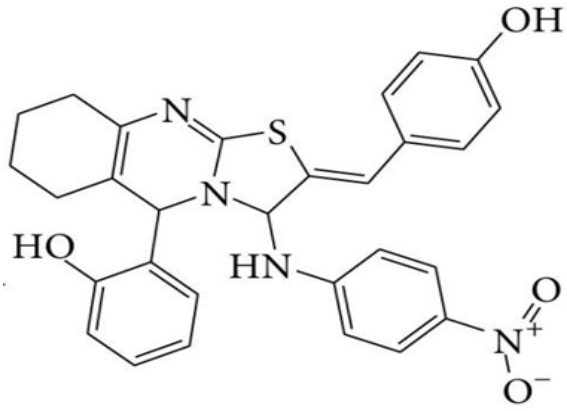


Fig 73

IV. CONCLUSION

In conclusion, the extensive investigation of various quinazoline derivatives and their analogues over the past decades highlights their sustained relevance in medicinal chemistry. Among the broad spectrum of pharmacological activities explored, anticancer and antimicrobial activities remain the most intensively studied and experimentally accessible, reflecting both their clinical necessity and the practicality of biological evaluation. This review compiles nearly two decades of scientific advancements, emphasizing the systematic exploration of structural modifications within the quinazoline nucleus and their profound influence on biological activity. These structure–activity insights have led to the identification of numerous potent and selective quinazoline-based candidates. Beyond their well-established anticancer potential, quinazoline scaffolds demonstrate remarkable therapeutic versatility, including anti-inflammatory, antioxidant, antitubercular, antimalarial, and enzyme inhibitory properties. Collectively, the compiled findings reaffirm that the quinazoline nucleus represents a robust, adaptable, and highly valuable scaffold for rational drug design.

Furthermore, strategic modifications of the quinazoline core—such as heterocyclic fusion, bioisosteric replacement, hybridization strategies, and targeted substitution at key positions—have significantly enhanced pharmacological profiles, offering a promising template for future drug discovery. The structural flexibility and molecular tunability inherent to quinazoline scaffolds position them as exceptional candidates for the development of next-generation therapeutics. Moving forward, the integration of innovative synthetic methodologies, computational drug design, and mechanism-driven biological evaluation is expected to accelerate the translation of quinazoline-based molecules into clinically relevant applications. Overall, the insights summarized in this review not only reinforce the therapeutic significance of quinazoline derivatives but also provide a strong foundation for guiding future research toward fully realizing their broad pharmacological potential.

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