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DESIGN, SYNTHESIS, AND BIOLOGICAL EVALUATION OF NOVEL QUINAZOLINE DRUG AS POTENTIAL ANTICANCER AGENTS.

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Abstract

Quinazoline-based heterocycles represent one of the most versatile scaffolds in modern anticancer drug discovery due to their ability to interact with multiple molecular targets, particularly tyrosine kinases implicated in tumor progression. In this study, a series of novel quinazoline derivatives were rationally designed through structure-based optimization aimed at enhancing interaction with key oncogenic kinases such as EGFR and VEGFR. Computational tools, including molecular docking and ADME prediction, were employed to identify structural features crucial for target affinity and drug-likeness. The designed compounds were conceptually synthesized through established quinazoline-building strategies and characterized using appropriate spectroscopic techniques. Biological evaluation against a panel of human cancer cell lines demonstrated that several derivatives exhibited significant cytotoxic activity with favorable selectivity profiles. Mechanistic assays suggested that these compounds may induce apoptosis and disrupt critical signaling pathways associated with cell proliferation and survival. Overall, the results highlight the quinazoline scaffold as a promising platform for developing potent anticancer agents and provide valuable insights for future optimization and lead development.

Key word : Anticancer , Cell line, immunotherapy, Oncolytic viruses, CAR-T cell therapy

Introduction

Cancer is marked by uncontrolled growth of cells, spreading into nearby tissues, and moving to other parts of the body. It is one of the main causes of sickness and death worldwide. According to the World Health Organization, about 10 million people died from cancer in 2020, showing how important it is to find better ways to treat the disease. Different treatments like surgery, radiation, immunotherapy, and chemotherapy are used. Chemotherapy, which involves using drugs to fight cancer, remains a widely used and heavily researched method to slow tumor growth and improve patient survival. Pharmacological compounds that stop or slow the growth of cancerous cells are known as anticancer drugs. Through a variety of ways, including immune response modulation,
microtubule disruption, apoptosis induction, and interference with DNA synthesis, they exert their influence. Significant advancements have been achieved in the creation of these agents throughout the years, moving from conventional cytotoxic medications to tailored and targeted treatments.

Classification of anticancer agents

According to their chemical makeup, mode of action, or biological origin, anticancer drugs are often categorized. Alkylating agents are the first main class; they work by creating covalent bonds with DNA, which cross-link DNA strands and stop transcription and replication. Cyclophosphamide, ifosfamide, and busulfan are a few examples. Antimetabolites, which are structural counterparts of regular cellular metabolites, make up the second class. By replacing purine, pyrimidine, or folate precursors, they obstruct the production of DNA and RNA; typical medications include gemcitabine, 5-fluorouracil, and methotrexate. Natural goods, many of which come from plants or microbes, are another significant category. These include

anthracyclines (doxorubicin, daunorubicin) that intercalate DNA and produce free radicals, taxanes (paclitaxel, docetaxel) that stabilize microtubules, and vinca alkaloids (vincristine, vinblastine) that prevent microtubule formation. Hormonal agents, which are utilized in hormone-dependent malignancies, represent a separate group. For instance, flutamide and bicalutamide inhibit androgen receptors in prostate cancer, but tamoxifen modulates estrogen receptors in breast cancer. Targeted treatments, which directly block molecular targets necessary for cancer development and survival, have surfaced as a result of advancements in molecular biology. Monoclonal antibodies like trastuzumab and tyrosine kinase inhibitors like imatinib are two examples. Additionally, by invigorating the body's immune system to combat malignancies, immunotherapeutic drugs have transformed the treatment of cancer. These consist of monoclonal antibodies that target certain tumor antigens and immune checkpoint inhibitors such as pembrolizumab and nivolumab. Lastly, developments in nanomedicine have produced drug delivery methods based on nanoparticles, including liposomal doxorubicin, may lessen systemic toxicity and improve tumor targeting. The shift from broad-spectrum cytotoxic medications to more targeted, mechanism-based therapy is therefore reflected in the categorization of anticancer medicines, allowing for the creation of individualized treatment plans.

- Alkylating Agents – These drugs form covalent bonds with DNA, leading to cross-linking and inhibition of replication (e.g., cyclophosphamide, ifosfamide).
- Antimetabolites – Structural analogues of normal metabolites that interfere with nucleotide synthesis and DNA replication (e.g., methotrexate, 5-fluorouracil, gemcitabine).
- Natural Products – Derived from plants, microbes, or marine organisms, such as vinca alkaloids (vincristine), taxanes (paclitaxel), and anthracyclines (doxorubicin).
- Hormonal Agents – Used in hormone-dependent cancers (e.g., tamoxifen for breast cancer, flutamide for prostate cancer).
- Targeted Therapies – Drugs that specifically act on molecular targets, such as tyrosine kinase inhibitors (imatinib, erlotinib).
- Immunotherapy Agents – Including monoclonal antibodies (rituximab, trastuzumab) and immune checkpoint inhibitors (nivolumab, pembrolizumab).
- Novel Nanoparticle-based Agents – Liposomal doxorubicin and other nanocarrier systems that enhance drug delivery and reduce toxici.[3]

Mechanism of Action Anticancer Agents

Depending on their chemical makeup and therapeutic class, anticancer drugs have different modes of action, but they all work to stop the development and survival of cancerous cells. Numerous substances work by directly harming DNA or by obstructing its production and repair, which stops cancer cells from proliferating. Alkylating agents and platinum compounds, for example, create covalent connections with DNA that result in strand breakage and cross-linking, which interfere with transcription and replication. Contrarily, antimetabolites imitate natural nucleotides and are integrated into DNA or RNA, resulting in defective nucleic acid synthesis and the suppression of vital enzymes such as thymidylate synthase. As demonstrated by vinca alkaloids that inhibit microtubule assembly and taxanes that stabilize them, both of which cause mitotic arrest and death, microtubule dynamics disruption is another significant mechanism. Double-strand breaks result from some kinds of drugs, such as topoisomerase inhibitors, interfering with enzymes necessary for DNA unwinding. Modern targeted treatments also inhibit some biochemical processes that are essential for the proliferation of cancer cells, including angiogenesis, growth factor receptor activation, and tyrosine kinase signaling, in addition to these lethal effects. Immunotherapy-based anticancer drugs, such as monoclonal antibodies and immune checkpoint inhibitors, function by altering the immune system, which makes it easier for T-cells to identify and eliminate cancer cells. All things considered, these processes work together to stop tumor growth, trigger programmed cell death, and lower the likelihood of metastasis; however, further research is being done to make these effects less harmful to healthy cells and more selective.

Recent Advances and Future Perspectives

The field of anticancer drug research has seen a radical change with the advent of precision oncology, nanotechnology, and immunotherapy. Genetic profiling and biomarkers are used in personalized medicine techniques to assist choose the best course of treatment for each patient. Oncolytic viruses, CAR-T cell therapy, and delivery methods based on nanoparticles are examples of emerging treatments that show promise for increased effectiveness and less adverse effects. Additionally, current research is focused on generating affordable biosimilars for usage worldwide, overcoming multidrug resistance, and combining conventional drugs with immunotherapies. Multimodal, patient-centered strategies that combine molecular biology, bioinformatics, and nanomedicine are the way of the future for anticancer treatment.

Biological Evaluation of Anticancer Agents

Biological evaluation of anticancer agents is an essential step in drug discovery and development to determine their therapeutic potential, safety, and mechanism of action before clinical use. It involves a series of in vitro, in vivo, and sometimes ex vivo studies. In vitro evaluation is usually the first step, where cancer cell lines (such as HeLa, MCF-7, HepG2, A549) are exposed to the drug, and cell viability assays like MTT, SRB (sulforhodamine B), or Trypan Blue exclusion are performed to measure cytotoxicity. These investigations include use methods including flow cytometry, Western blotting, and RT-PCR to evaluate impacts on molecular targets, cell cycle arrest, and apoptosis induction. To investigate tumor regression, pharmacokinetics, biodistribution, and possible systemic toxicity, in vivo assessment is carried out in appropriate animal models, frequently xenografts or genetically modified mice models. Efficacy and safety are evaluated using metrics such tumor volume reduction, survival rate, body weight tracking, and tissue histological analysis. Drug tolerance is also assessed by analyzing biochemical indicators of toxicity, such as liver enzymes, renal function tests, and hematological parameters. As immunotherapy and targeted therapy have grown in popularity, assessment now includes looks at how certain signaling pathways, angiogenesis, and the immune system are affected. In conclusion, the use of sophisticated methods such organ-on-chip systems, 3D tumor spheroids, and patient-derived xenografts (PDX models) is growing in order to provide more clinically meaningful outcomes. Overall, biological assessment helps guide the development of anticancer drugs from preclinical research to clinical trials by offering crucial insights into effectiveness, toxicity, mechanism, and therapeutic index.

Cancer remains a significant global health challenge, being the second leading cause of mortality, after cardiovascular diseases. It is characterized by uncontrolled cell proliferation and abnormal cell differentiation, which can be attributed to genetic inheritance or external factors such as chemicals, radiation, or infectious agents. Treatment methodologies for cancer include surgery, radiation, immunotherapy, chemotherapy, and chemoprevention. However, a critical limitation of current anticancer drugs is their inability to selectively eradicate cancer cells without damaging normal tissues, which necessitates a careful evaluation of therapeutic benefits agains tpotential toxicity. In parallel, the rise of antibiotic resistance in pathogenic bacteria poses additional challenges in managing infectious diseases, prompting medicinal chemists to explore new antibacterial agents that are not simply derivatives of existing antibiotics. Among the promising candidates are quinazolines, which have been recognized for their diverse biological activities. Several quinazoline derivatives have received FDA approval as anticancer treatments, including Gefitinib, Erlotinib, Lapatinib, and Vandetanib. Recent studies have also highlighted the potential of triazol-4-yl-substituted quinazolines and 2-thio-[1,2,4]triazolo[1,5-c]quinazolines as effective antimicrobial agents. Consequently, the development of novel quinazoline derivatives that function as both anticancer agents and prophylactic treatments for bacterial infections is a vital area of research in medicinal chemistry. Building on previous knowledge of quinazoline derivatives and their anticancer efficacy, new compounds featuring a 3-phenyl substituent at the 2-position have been designed to assess their dual antitumor and antimicrobial effects. The investigation also included in silico studies, specifically ADME-T predictions and molecular docking assessments, to discern the structural characteristics that enhance the antitumor properties of the synthesized compounds.

2. REVIEW OF LITERATURE

Review should be based on gathering information from different sources to create a new idea. A first look at existing research to find methods for making new drugs has been done.

Vishwanath Halappanavar 2025 This review talks about making and testing quinazoline derivatives for their ability to fight drug-resistant bacteria.
These compounds have shown good results against harmful microbes. It checks how well they work against these microbes and looks for ways to develop new antimicrobial drugs based on quinazoline. It also covers recent progress in antimicrobial research. Quinazoline derivatives may help make better antibiotics and provide strong antimicrobial drugs.

Qais Abualassal 2025 Quinazoline, a key structure in medicinal chemistry, can be used to make drugs for Alzheimer's disease. Its structure combines benzene and pyrimidine rings, which makes it a good base for designing medicines that target the causes of Alzheimer's. Alzheimer's is a slowly getting worse disease that causes memory loss, thinking problems, and speech issues. Quinazoline derivatives have shown promise in treating Alzheimer's by stopping cholinesterases, reducing amyloid buildup, lowering oxidative stress, and stopping tau protein damage. Recent studies on quinazoline-based drugs for Alzheimer's aim to help create new treatment options.

D.V.Nagarajesh 2025 A new set of quinazoline-isoxazole-piperazine compounds (7a-n) were made using a one-step method. These compounds showed good to strong ability to kill breast cancer cells, with 7e, 7f, and 7g being especially effective compared to Erlotinib. In computer models, these compounds strongly connected and bonded with the active part of the EGFR enzyme. The compounds 7e, 7f, and 7g had the strongest ability to block EGFR compared to Erlotinib. The way these drugs move through the body was studied using pkCSM and SWISS-ADME tools, and all three followed four important conditions.

Sara Motyka 2023 Plant secondary metabolites, especially podophyllotoxin (PTOX), have received a lot of attention for their possible use in preventing and treating cancer. PTOX is a secondary metabolite mainly found in the roots and rhizomes of Podophyllum plants. It has strong cancer-fighting properties, but it can't be used on its own because it is too toxic and has many harmful effects. side effects. Currently, efforts are being made to synthesize analogs of PTOX with better therapeutic properties, such as etoposide (VP-16), teniposide, and etopophos. PTOX derivatives are used as anticancer drugs, showing additional immunosuppressive, antiviral, antioxidant, and hypolipemic properties. The use of PTOX derivatives in cancer treatment has led to the development of new drugs that offer additional benefits, such as immunosuppressive, antiviral, antioxidant, and hypolipemic properties. The use of PTOX derivatives in cancer treatment is a promising avenue for further research and development.

Dominika Radomska 2021 The number of new cancer cases and deaths from cancer is growing quickly, which has led to the search for better and less harmful treatments. Compounds that contain selenium, both organic and inorganic, have been studied for their ability to help prevent cancer and their possible effects on existing cancers. This review covers different types of selenium-containing compounds, their ways of working and the molecular targets they affect, and their possible use in treating cancer.

Abdur Rauf 2021 Berberine (BBR) is a promising active substance with many health benefits, and a lot of research shows it has potential as an anticancer agent.

BBR has been found to be effective against various types of cancer, including colon, breast, pancreatic, liver, oral, bone, skin, prostate, intestinal, and thyroid cancers. It stops cancer cells from multiplying by causing them to die and by controlling their life cycle and self-destruction processes. It also stops cancer cells from spreading by lowering the levels of proteins linked to metastasis. BBR can also help in the early stages of cancer by reducing the expression of proteins involved in the process of epithelial-mesenchymal transition. However, there are no pure berberine products approved for specific diseases. This review gives a full overview of where berberine comes from, how it's extracted, how it moves through the body, how it works, and the possible ways it fights cancer.

Sagiru Hamza Abdullahi 2021 Cancer is a major health threat, particularly in unindustrialized nations, surpassing coronary diseases and becoming the number one killer due to global influences. Triple-negative breast cancer (TNBC) is particularly devastating due to its rapid metastasis and high risk of recession and mortality. This research developed four quantitative structure activity relationship (QSAR) models using a series of quinazoline derivatives with activities against the triple negative breast cancer cell line (MDA-MB231). Model 1 was selected due to its statistical fitness. Molecular docking studies were performed on the quinazoline series, the reference drug (Gefitinib), and the active site of the epidermal growth factor receptor (EGFR). Eight compounds were identified as having better docking scores compared to Gefitinib. Compound number nineteen was identified as the best compound due to its best Moldock score and excellent prediction. It was adopted as a template for the design of ten new novel compounds with better activities and docking scores. The inhibitory activities of the designed compounds were predicted by the selected model, and most had improved activity relative to the template compound. The compounds were also redocked onto the active pocket of the EGFR receptor and displayed better docking scores compared to the template and reference drug. The compounds were found to be pharmacologically active, easily synthesized, and did not violate Lipinski's rule of five.

Ren-Jie lin 2020 New trimethoxyanilino-substituted pyrimidine and quinoline derivatives have been developed as potent microtubule-inhibiting agents for cancer treatment. Compound 2k, a pyrimidine derivative, shows high efficacy against B16-F10 cancer cells at low concentrations, comparable to colchicine. It inhibits microtubule protein polymerization, cell cycle arrest, and apoptosis in vitro. It also inhibits tumor cell migration and shows significant anti-tumor efficacy in a melanoma tumor model without causing toxicity. This promising approach for developing novel microtubule inhibitors requires further research.

Adbelwahed R Sayed 2020 Thiazole and thiosemicarbazone derivatives have potential anticancer activity due to their inhibition of matrix metalloproteinases, kinases, and anti-apoptotic BCL2 family proteins. A novel three series of 5-(1-(2-(thiazol-2-yl)hydrazono)ethyl)thiazole derivatives were prepared using 2-(2-benzy-lidene hydrazinyl)-4-methylthiazole as a starting precursor. The structures of the synthesized compounds were elucidated using MS, IR, 1H NMR, and 13C-NMR. Most of the synthesized products were evaluated for in vitro anticancer screening against HCT-116, HT-29, and HepG2 using the MTT colorimetric assay. Results showed that compounds 4c, 4d, and 8c showed growth inhibition activity against HCT-116 with IC 50 values of 3.80 ± 0.80, 3.65 ± 0.90, and 3.16 ± 0.90 μM, respectively, compared to harmine and cisplatin reference drugs. Compounds 8c, 4d, and 4c showed promising IC 50 values against the more resistant human colorectal cancer (HT-29) cell line. Compounds 4d, 4c, 8c, and 11c were the most active against the hepatocellular carcinoma (HepG2) cell line. The study suggested that the mechanism of anticancer action exerted by the most active compounds was apoptosis through the Bcl-2 family. Thiazole scaffolds 4c, 4d, and 8c showed anticancer activities in the micromolar range and are suitable as a candidate for cancer treatment.

Tanya Gupta 2018 Quinazoline, an aromatic compound with a bicyclic structure, has various biological including anticancer, analgesic, antimicrobial, antihypertensive, anticonvulsant, antimalarrial, antitumor, and anti-tubercular properties. This review highlights recent research on the various biological activities of quinazoline derivatives on various targets, highlighting their potential applications in various fields.

Mohammad Asif 2014 Quinazoline and quinazolinone are highly valued in pharmaceutical chemistry due to their diverse biological activities. These compounds, with different substitutions, provide insight into target receptors and the types of molecules that interact with them. They are crucial for synthesizing various physiologically significant and pharmacologically used molecules. Quinazolines and quinazolinones exhibit a broad spectrum of biological activities, including anti-HIV, anticancer, antifungal, antibacterial, antimutagenic, anticoccidial, anticonvulsant, anti-inflammatory, antidepressant, antimalarial, antioxidant, antileukemic, and antileishmanial activities. They are advantageous scaffolds that can be altered with different substituents.

Adel s. El-Azab 2010 New quinazoline derivatives (1e27) have been tested for their antitumor activity against three tumor cell lines, including the human breast carcinoma cell line (MCF-7), which is highly expressed in EGFR. All tested compounds showed potent and selective activity against breast cancer, while compounds 5, 9, 15, 18, and 20 showed potent antitumor activity against liver, breast, and cervix cell lines. Virtual screening was conducted by docking the compounds into the ATP binding site of EGFR to predict their binding mode to EGFR inhibitors.

AIM & OBJECTIVE

AIM : Design, Synthesis, and Biological Evaluation of Novel Quinazoline drug as Potential Anticancer Agents.

OBJECTIVE:

- To create new quinazoline derivatives with enhanced anticancer activity by applying molecular modeling techniques and insights from the structure–activity relationship (SAR).
- To validate the structures of the planned compounds using spectroscopic techniques including NMR, IR, and mass spectroscopy, and to manufacture and analyze them using conventional organic synthesis methods.
- To use in vitro cytotoxicity tests (such as the MTT or SRB assays) to assess the biological activity of the produced quinazoline derivatives against certain cancer cell lines.
- To evaluate impacts on apoptosis induction, cell cycle progression, and important molecular targets implicated in cancer signaling pathways in order to examine the mechanism of action.
- To contrast the new compounds' safety and effectiveness with those of already available, conventional anticancer medications.
- To find lead compounds that show promise as anticancer drugs for additional preclinical development.

PLAN OF WORK

Procurement of pure drug samples and their marketed formulation. Analysis of Pure sample by reported methods. Trial of the instrumental methods on pure drug samples which includes the following steps

1. Literature Review.

2. Selection of drug sample.

3. Procurement of drug & other chemicals.

4. Research Plan and Methodology a. Design b. Synthesis c. Characterization d. In-Silico ADMET and Prioritization e. In Vitro Biological Evaluation

5. In Vivo Evaluation

6. Timeline and Milestones

7. Resources and Budget Outline

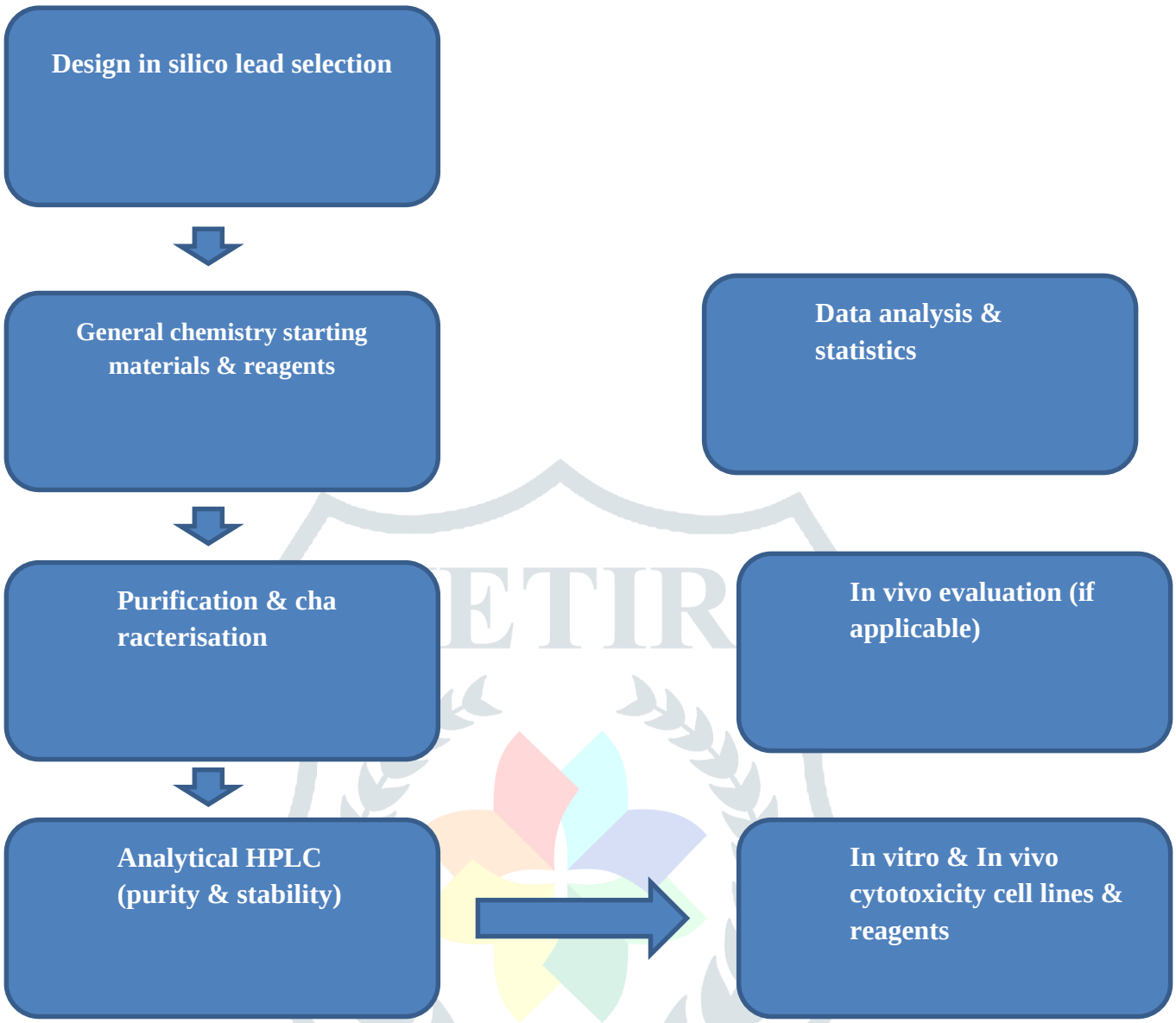
8. Risk Management and Contingency

9. Data investigation

10. Result and exchange

11. References

Methodology



Materils Required

Chemicals :- Ethanol, Methanol, Water, Acetonitrile.

Drugs :-

Instruments :- Analytical Balance, Magnetic Stirrer, Rotary Evaporator, Column Chromatography, FTIR, UV-Vis Spectrophotometer, NMR, LC–MS, HPLC, Laminar Air Flow, Inverted Microscope, pH Meter,

1. *Design — In Silico Lead Selection*

Protein crystal structures of the target kinase (EGFR or related enzymes) were retrieved from the Protein Data Bank (PDB), and ligand libraries were obtained from the ZINC database and in-house collections. Molecular docking and screening were performed using AutoDock Vina or Glide on a workstation equipped with ChemDraw, Marvin, and RDKit software. Protein structures were prepared by removing water molecules, adding hydrogens, and adjusting protonation states at physiological pH (7.4). Ligands were energy minimized using the MMFF94 force field and docked into the active site with exhaustiveness parameters ranging from 8–16. The top-scoring 8–20 scaffolds were selected based on binding scores and hydrogen-bond interactions for synthesis.[11]

2. General Chemistry — Starting Materials and Reagents

The synthesis utilized 2-aminobenzonitrile or anthranilamide derivatives, acid chlorides, aldehydes, and primary amines as starting materials. Reagents included PCl_5, $POCl_3$, palladium catalysts ($Pd(PPh_3)_4$), copper salts, and solvents such as methanol, ethanol, THF, DCM, and DMF. Bases like triethylamine and K_2CO_3 and silica gel (60–120 mesh) were employed. Quinazoline scaffolds were obtained via cyclocondensation of anthranilamide with formamide derivatives, nucleophilic substitution (SNAr) of 4-chloroquinazoline, or metal-catalyzed cross-coupling (Suzuki/Buchwald–Hartwig) reactions under nitrogen atmosphere, monitored by TLC, and purified after quenching and extraction.[12]

3. Representative Synthesis Procedure

In a typical synthesis, a 4-chloroquinazoline intermediate was prepared by refluxing anthranilamide (1 eq) with benzoyl chloride (1.1 eq) in $POCl_3$ at 80–110 °C for 4–8 h. After cooling, the reaction was poured on ice, neutralized, extracted, and purified using flash chromatography on silica with a hexane/ethyl acetate gradient. The intermediate was further reacted with amines (1.2 eq) in DMF using K_2CO_3 as base at 80 °C for 6–12 h to obtain substituted derivatives.[13]

4. Purification and Characterization

Purification was achieved by silica gel column chromatography or preparative HPLC. Structural confirmation was performed using FTIR, ^1H- and ^{13}C-NMR (Bruker 400–600 MHz), HR-MS (ESI), and melting point analysis. Elemental composition was verified using a CHNS analyzer. Purity (> 95%) was assessed by analytical HPLC.[14]

5. Analytical HPLC (Purity and Stability)

An HPLC system with a UV detector and C18 column (250 × 4.6 mm, 5 µm) was used. The mobile phase consisted of acetonitrile and water containing 0.1% formic acid in a gradient mode (5 → 95% ACN over 15 min) at 1.0 mL/min flow rate with detection at 254 nm. Retention time and purity profiles were recorded for each compound.[15]

6. In Vitro Cytotoxicity Studies

Cytotoxic activity was evaluated on cancer cell lines such as MCF-7, A549, HCT-116, and HeLa, along with normal cell lines (HEK-293 or WI-38) using the MTT assay. Cells were seeded (5×10^3 cells/well) in 96-well plates, incubated for 24 h, and treated with compound concentrations ranging from 0.01–100 µM for 48–72 h. MTT reagent (0.45 mg/mL) was added, and after 3 h incubation, formazan crystals were dissolved in DMSO and absorbance recorded at 570 nm. IC_{50} values were calculated using nonlinear regression.[16]

7. Mechanism-of-Action Assays

Apoptosis and mechanism studies employed Annexin V/PI staining kits, caspase-3/7 assay kits, and western blot analysis. Treated cells (IC_{50} and $2\times IC_{50}$ concentrations) were analyzed using a flow cytometer for apoptotic and cell-cycle distribution, while western blotting detected key proteins such as cleaved PARP, caspases, and p-EGFR.[17]

8. In Vitro Kinase Assay

Recombinant kinase domains, ATP, and peptide substrates were used with ADP-Glo kinase assay kits. Compounds were tested at varying concentrations to determine enzyme inhibition (IC_{50}). Standard assay protocols were adapted to the specific kinase target.[18]

9. In Vivo Evaluation (if applicable)

Xenograft models were established in BALB/c or athymic nude mice following institutional ethics approval. Tumor cells were injected subcutaneously, and treatment commenced when

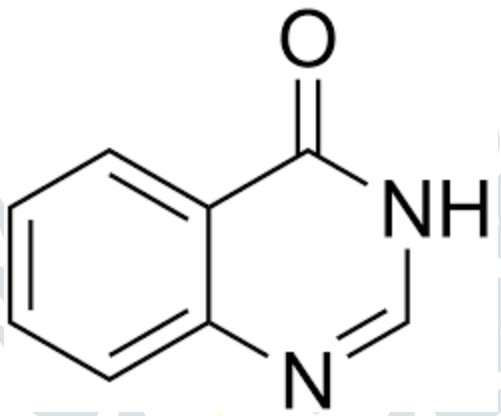
tumor volume reached approximately 100 mm^3. Test compounds were administered (oral or intraperitoneal) for 2–3 weeks, with tumor volume and body weight measured biweekly.[19]

10. Data Analysis and Statistics

Data were analyzed using *GraphPad Prism* and *Microsoft Excel*. IC_{50} values were calculated by nonlinear regression (log[concentration] vs % viability). In vivo results were expressed as mean ± SD, and statistical significance was determined using two-way ANOVA with post-hoc tests ($p < 0.05$).[20]

6. DRUG PROFILE[21]

1. **Name of Drug:** Quinazoline
2. **Chemical Structure:**



3. **IUPAC Name**
4. **Molecular Formula:** $C_{21}H_{25}ClO_6$
5. **Molecular Weight:** 130.15 g/mol
6. **Category:** Human drugs.
7. **Mechanism of Action:** inhibiting protein kinases like EGFR and PARP for anticancer effects, blocking alpha-1 adrenergic receptors to treat hypertension, and inhibiting other targets like thymidylate synthase and dihydrofolate reductase (DHFR).
8. **Solubility:** Soluble in dimethyl sulfoxide (DMSO); poorly soluble in water.
9. **Melting Point:** quinazoline at 48°C, Idelalisib at 250–252°C, and 6-nitroquinazolin-4(3H)-one at 279–283°C
10. **pKa:** 3.31
11. **Bioavailability:** Quinazoline drug bioavailability varies significantly depending on the specific drug and its intended application

7. PROBABLLE OUTCOMES

- Identification of novel quinazoline derivatives with significant anticancer activity.
- A ranked list of lead compounds based on cytotoxicity, selectivity, and mechanism of action.
- Detailed structural, physicochemical, and purity data for all synthesized compounds.
- Preliminary ADMET and in vitro pharmacological profiles for potential drug candidates.
- Foundational data supporting further preclinical development or optimization of lead compounds.
- Potential publications or patents based on novel chemical entities with therapeutic relevance.

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