QUINAZOLINE: UNIQUE AND VERSATILE PHARMACOPHORE IN THE FIELD OF CANCER
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Abstract:
Quinazolines are the most important class of heterocyclic compounds. Quinazoline is a bicyclic compound consisting of a pyrimidine system fused at 5, 6 with benzene ring. Quinazoline is considered as an important chemical synthesis of various physiological significance and pharmacological utility. Cancer is a disease characterized by uncontrollable, irreversible, independent, autonomous, uncoordinated and relatively unlimited and abnormal over growth of tissues. The drugs containing Quinazoline groups were the first effective chemotherapeutic agents which were systematically proved for the prevention and cure of bacterial infection in human beings. Literature revealed that Quinazoline derivatives may serve as an important model on as potent anti-cancer agent. When one biological active molecule is linked to another, resultant molecule generally has increased potency. Most of the derivatives showed enhanced anti-cancer activity. So, Quinazoline derivatives can serve as future therapeutic leads for the discovery of anti-cancer drugs. This review was focused on the Quinazolines and its different derivatives that posses anticancer activities.

Keywords: Quinazolines, Cancer, Cytotoxic Activity, Antiproliferative Activity, Antitumor activity.

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INTRODUCTION:
Heterocyclic chemistry is a chemistry involving the heterocyclic compounds which contain atoms of at least two different elements as number of ring. The heterocyclic may be inorganic, though the compound has carbon atoms in the ring, the word hetero means different from carbon and hydrogen. Nitrogen containing heterocyclic compounds plays an important role in medicinal chemistry. Quinazolines are a large class of active chemical compounds exhibiting a broad spectrum of biological activities in animals as well as in humans. Literature studies on quinazolines have shown that these derivatives possess a wide variety of biological activities such as antidiabetic[1], antiviral[2], antibacterial[3], anticonvulsant[4], anti-inflammatory[5], CNS depressant[6], antimalarial[7], antimicrobial[8], antifungal[9], antioxidant[10], anthelmintic[11] activity.
Quinazoline is one of the most important heterocyclic compound, weak base, having varied biological activities and still of great scientific interest now a days. They are widely found in bioorganic and medicinal chemistry with application in drug discovery. This review was focused on the Quinazolines and its different derivatives that posses anticancer activities.

Anticancer activity of Quinazoline derivatives:
A novel 3-(substituted benzylideneamino)-7-chloro-2-phenyl quinazoline-4(3H)-one has been synthesized by Malleshappa N. Noolvi and Harun M. Patel. Rational approach and QSAR techniques enabled the understanding of the pharmacophoric requirement for 2,3,7-tri substituted quinazoline derivatives to inhibit EGFR-tyrosine kinase as antitumor agents and could be used as an excellent framework in this field that may lead to discovery of potent anti tumor agent [12].

Salman et al worked on the Design, synthesis and biological evaluation of Novel Quinazoline Derivatives. Some of the synthesized compounds were screened for human liver cell line (HepG2) activity[13].

New Quinazoline derivatives were synthesized by Salman et al. All newly synthesized compounds were screened for their anticancer studies. The results revealed that some of the synthesized compounds have a significant biological activity as anticancer agents[14].

A series of N mustard-quinazoline conjugates was synthesized by B. Marvania et al and subjected to antitumor studies. The preliminary antitumor studies revealed that these agents exhibited significant antitumor activity in inhibiting various human tumor cell growths in-vitro[15].
Bhavesh Prajapati et al synthesized Morpholino Propoxy Quinazoline Derivatives. All synthesized compounds were tested for their cytotoxicity by MTT assay. Among all the synthesized derivatives, compound-II was shown promising anticancer activity as compared to other synthesized derivatives[16].

Manish Chaudhari et al synthesized some of the Novel Quinazoline Derivatives and screened for the Anticancer and Anti-Microbial activities[17].

Renata Ovadekova et al studied the Cytotoxicity and Detection of Damage To DNA By 3-(5–Nitro-2-Thienyl)–9–Chloro–5–Morpholin–4–Yl[1,2,4]Triazolo[4,3-C]Quinazoline On Human Cancer Cell Line HeLa. A new synthetically prepared quinazoline derivative was the most effective derivative in our primary cytotoxic screening. In this study, we evaluated cytotoxic/antiproliferative activity of NTCHMTQ using human tumor cell line HeLa[18].

Asmaa A. Magd-El-Din et al carried out the Synthesis of Potent Antitumor Oxo Quinazoline, Pyrazole and Thiazine Derivatives. Compounds were tested against sixteen different human cancer cell lines and most of the compounds were superior to the familiar comparative standards[19].
S.N. Manjula, et al were synthesized novel Quinazoline derivatives. These were evaluated for their anti-tumor activity against Ehrlich ascites carcinoma (EAC) and two different concentrations were evaluated for their antitumor activity against Dalton’s ascites lymphoma (DLA) bearing Swiss albino mice [20].

A variety of novel 2-(1-substituted-piperidine-4-ylamino)quinazoline derivatives were prepared WANG Yong-kang, et al, and their antiproliferative activities on five cancer cell lines were evaluated by MTT assay [21].

Tetrazolo[1,5-c]quinazoline-5-thione S-Derivatives have been synthesized by L. M. Antypenko et al. The substances were screened for antibacterial and antifungal activities. The substances were screened for their ability to inhibit 60 different human tumor cell lines [22].

N-(4-chlorophenyl)-5,6,7-trimethoxyquinazolin-4-amine dihydrochloride were synthesized by Huang et al. The anticancer activities of N-(4-chlorophenyl)-5,6,7-trimethoxyquinazolin-4-amine dihydrochloride against four kinds of cell lines were evaluated by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay [23].

A series of 3,4-dihydroquinazoline derivatives were studied by Gi Hyun Kwon et al with anti-cancer activities against human colon cancer HT-29 cell were subjected to three-dimensional quantitative structure-activity relationship (3D-QSAR) studies using the comparative molecular similarity indices analysis (CoMSIA) approaches [24].

Synthesis of some new quinazoline derivatives were reported by K. Manasa et al. All the synthesized compounds have been screened for their antioxidant and anticancer activity [25].
Novel derivatives of quinazoline have been synthesized by A.S. El-Azab et al and tested for their antitumor activity against three tumor cell lines among these cell lines the human breast carcinoma cell line (MCF-7) in which EGFR is highly expressed. All tested compounds showed potent and selective activity against breast cancer (MCF-7) with IC50 range of 3.35e6.81 mg/ml [26].

Two new synthesized and characterized quinazoline Schiff bases were investigated for anticancer activity against MCF-7 human breast cancer cell line by Fadhil Lafta Faraj et al. Results showed significant activity towards MCF-7 cells via either intrinsic or extrinsic mitochondrial pathway and are potential candidate for further in-vivo and clinical breast cancer studies [27].

CONCLUSION:
Quinazoline exhibits a wide range of biological properties due to its potent biological activities. It is a versatile tool in the field of cancer amongst all activities. It produces anticancer activities not only by interacting with heterocyclic ring but also through various inorganic complexes. It can be concluded that this class of compounds certainly holds great promise towards good active leads in medicinal chemistry. A further study to acquire more information concerning pharmacological activity is in progress. The biological profiles of these new generations of Quinazolines represent much progress with regard to the older compounds. Hence this unique molecule must act like a boon in the field of developing various synthetic anticancer agents.

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