2. LITERATURE REVIEW

Several structural modifications on the quinazoline nucleus were done to enhance the biological activities, like analgesic, anti-inflammatory, anticonvulsant, antibacterial, antifungal, antitubercular and antihistaminic activity, which attracted the attention of medicinal chemists\textsuperscript{18-25}. Herein a detailed literature survey is described on the structural modifications of the quinazoline nucleus with their biological activities.

2.1 ANTIHISTAMINIC ACTIVITY

A series of 1,3,4-triazolo quinazolin-4-ones (1) by placing 4-substituted piperazinyl moiety at 1\textsuperscript{st} position with the aim provide antihistaminic activity was synthesized. These compounds showed significant antihistaminic activity\textsuperscript{18}. Lemura and coworkers\textsuperscript{19} in 1989 synthesized the 2-(4-substituted piperazinyl methyl)-3-substituted quinazolin-4-ones (2) and studied their antihistaminic activity. Series of 2-amino-5,6,7,8-substituted quinazolines with substituted amino group (3) and amide group (4) at 4\textsuperscript{th} position were prepared and these compounds showed significant antiallergic activity\textsuperscript{26, 27}.

The derivatives of 3-(N,N-dialkylamino)-alkyl-2-phenyl-3,4-dihydro quinazolin-4(3H)-ones (5) were synthesized and evaluated for their H\textsubscript{1} antihistaminic activity. Among synthesized compounds 3-(N,N-dibutylamino)-propyl-2-phenyl-quinazolin-4(3H)-ones and 6-iodo-3-(N,N-dibutylamino)-propyl-2-phenyl-quinazolin-4-(3H)-one was found to be more potent\textsuperscript{28}.

The 6-substituted chromon-[2’,3’,6,7]-[1,3,4]-thiadiazepin-[2,3-b]-6’-substituted quinazolin-4(3H)-ones\textsuperscript{29} (6) were reported to exhibit significant inhibition of histamine induced contraction in guinea pig ileum in \textit{In-vitro} studies. Bromo substitution at 6’ position contributed towards the enhanced potency while 6-methyl substituent decreased the antihistaminic potency.
Spiro-isobenzofuranones/2-substituted piperidino quinazolin-4-ones were discovered as potent, selective and brain penetrable non-imidazole H₃ receptor inverse agonist by Jitsuoka et al. They identified a lead molecule by screening their compounds against the human H₃ receptor. Incorporation of quinazolinone as left hand portion of lead molecule (7) resulted in loss of activity.
Some novel derivatives of 2-[4-(amino alkoxy)-phenyl]-quinazolin-4(3H)-ones (8) as potent and selective histamine H₃ receptor inverse agonists was developed and the compound (8) was found to be potent inhibitor of human H₃ (hH₃) than standard compound. Alagarsamy et al., synthesized novel 4-(3-ethylphenyl)-1-substituted-4H-[1,2,4]-triazolo-[4,3-a] quinazolin-5-ones and these compounds showed significant H₁-antihistaminic activity. A series of 3-[(N,N-dialkylamino)alkyl]-6-halo-2-thio-4(3H)-quinazolines (9) were prepared and these compounds were found to possess H₁-antihistaminic activity.

### 2.2 ANTIHYPERTENSIVE ACTIVITY
A series of 2-substituted amino-5,6,7,8-substituted quinazolin-4-ones (10) were prepared in 1965 and these compounds exhibited antihypertensive activity by inhibiting the angiotensin converting enzyme\textsuperscript{34}.

In 1968, a series of 2,6,7-trisubstituted quinazolin-4-ones were synthesized and evaluated their antihypertensive activity. The compound 2-diethylamino-6,7-dimethoxy quinazolin-4-one\textsuperscript{35} (11) was found to be the most active agent in this series.

A series of 1,3,4-triazolo quinazolin-4-ones (12, 13) were synthesized and the compounds 1,2,9-trimethyl-1,3,4-triazolo quinazolin-4(3\textit{H})-one and 2,9-dimethyl-1,3,4-triazolo quinazolin-4(3\textit{H})-one exhibited potent antihypertensive activity\textsuperscript{36,37}. Similarly, a series of 1,2,4-triazolo quinazolines (14) showed antihypertensive activity ranging from 20.5 to 46.7\% with maximum activity when R was a thiol substituent\textsuperscript{38}.

And series of 4-substituted-1,2,4-triazolo quinazolin-4-ones (15) with the piperazine moiety at 1\textsuperscript{st} position was also exhibited antihypertensive activity\textsuperscript{39}. Arylamine substitution at 4\textsuperscript{th} position of the 1,7,8-trisubstituted-1,2,4-triazolo quinazolines (16) showed significant antihypertensive activity\textsuperscript{40}. Some 2,3-dihydro imidazo [1,2-c] quinazolines and substituted imidazo [1,2-c] quinazolines were reported to exhibit significant antihypertensive activity\textsuperscript{41}. 
Various series of quinazolin-2,4-diones with substitution at 3rd position (17, 18, 19) were synthesized and the compounds were found to exhibit significant antihypertensive activity\textsuperscript{42-45}.

In 1998, a series of fused quinazolines and 1,2,4-benzothiadiazine-1,1-dioxides were synthesized and these compounds shown significant $\alpha$-adrenergic antagonistic activity\textsuperscript{46}. In 1998, 2-methyl-3-[5-(substituted phenyl)-triazoline]-4(3$H$)-
quinazolinones\textsuperscript{47} (20) was reported as potential cardiovascular agents and the most potent member of this series is 2-methyl-[3-imino-(2-fluoro phenyl)]-4(3\textit{H})-quinazolinone. Alagarsamy\textsuperscript{48} \textit{et al.}, synthesized some novel 2-substituted[1,3,4]thiadiazolo[2,3-b]-6,7-disubstituted thieno [3,2-e]pyrimidin-5(4\textit{H})-ones (21) and evaluated their antihypertensive activity.

\begin{center}
\begin{tikzpicture}
\begin{scope}[every node/.style={draw, circled}]
\node (a) at (0,0) {17};
\node (b) at (2,1.5) {18};
\node (c) at (4,3) {19};
\node (d) at (6,4.5) {20};
\end{scope}
\begin{scope}[every node/.style={scale=0.5}]
\node (1) at (0,0) {\includegraphics[width=1\textwidth]{image1}};
\node (2) at (2,1.5) {\includegraphics[width=0.5\textwidth]{image2}};
\node (3) at (4,3) {\includegraphics[width=0.5\textwidth]{image3}};
\node (4) at (6,4.5) {\includegraphics[width=0.5\textwidth]{image4}};
\end{scope}
\end{tikzpicture}
\end{center}
A series of quinazolin-2,4-diones\(^{49}\) (22) with a substituted piperazine moiety at 3\(^{rd}\) position were prepared and these compounds were found to exhibit antihypertensive activity.

Some 2-substituted [1,3,4]thiadiazolo[2,3-b]quinazolin-5(4\(H\))-ones (23) and novel-3-benzyl-2-substituted-3\(H\)[-1,2,4]triazolo[5,1-b] quinazolin-9-ones (24) were reported as antihypertensive agents\(^{50, 51}\).

The test compound 3-benzyl-2-methyl-[1,2,4]triazolo[5,1-b]quinazolin-9(3\(H\))-one exhibited significant antihypertensive activity. A series of octahydroquinazoline\(^{52}\) (25) derived compounds were screened for their hypotensive activity and most of the compounds showed remarkable hypotensive activity.
2.3. ANTI-CANCER ACTIVITY

Some \( N\)-[4-(amino-3,4-dihydro-4-oxoquinazolyl)methyl]-\( N\)-prop-2-yl-amino]benzoyl-L-glutamic acid (26) and their derivatives were prepared as selective thymidylate synthetase inhibitors. These compounds showed encouraging antitumor activity against breast and ovarian cancer in clinical trials\(^{20}\). Some 2-methyl-6-substituted quinazolines\(^{21}\), 2,4-diamino-6-substituted quinazolines (27) and a series of benzimidazo[1,2-c]quinazolines were synthesised and these compounds were found to exhibit potent antitumor activity\(^{53, 54}\). A series of 3-chloro-\( N\)-[3,4-dihydro-2-methyl-4-oxo-6-quinazolinyl]methyl]-4-phenyl sulphonyl]-\( N\)-(prop-2-nyl)aniline\(^{55}\) and 4,5,6,7-tetra substituted quinazolines\(^{56}\) (28) were synthesized and these compounds were found to exhibit anticancer activity.

The synthesis of 4-arylamino-6,7-disubstituted quinazolines\(^{57}\) (29) and a series of 2,4-diamino-6-(aryl methyl)-5,6,7,8-tetrahydro quinazolines\(^{58}\) (30) were reported. These compounds were reported to exhibit antitumor activity.
Synthesis and their antitumor activity of some 3-(3-phenyl isoxazo-5-yl) quinazoline derivatives, 2,3-dihydro-3-methoxy-2-phenyl-4-quinazolinones, some novel fluorinated condensed quinazolines and series of benzothiazol-[2,3-b]-quinazoline derivatives were reported.

The synthesis, SAR and antitumor activity of a series of 4-substituted anilino-3-cyano-6,7-dimethoxy quinazolines was reported. A series of 4-(3-ethyl phenylamino) quinazolines were synthesized and patented for their anticancer activity.

of caspase 3 in murine leukemia L1210 cells, fibroblast NIH-3T3 cells and in human cancer cell line HeLa was reported\textsuperscript{66}.

![Chemical structures](image)

Novel biologically active thione moiety quinazoline derivatives showed antitumor activity\textsuperscript{67}. Asymmetric synthesis and potent fluorescent tubulin inhibition with anticancer activity\textsuperscript{68} of 2,3-dihydro-2-arylquinazolin-4-ones (35) was reported. A series of 6-bromo-2-(morpholin-1-yl)-4-anilinoquinazolines and N-(4-methoxy phenyl)-N-2-dimethyl quinazolin-4-amines (36), were synthesized and these compounds showed antiproliferative activity\textsuperscript{69-70}.

In 2010, a series of novel 3-(1,3,4-thiadiazol-2-yl)-quinazolin-4(3H)-ones and 3,4-dihydro quinazoline dihydrochloride (37) were synthesized and these compounds showed anticancer activity\textsuperscript{71, 72}. Highly functionalized 2,4-diamino quinazolines (38) and their derivatives showed anticancer and anti-HIV activity\textsuperscript{73}. 
Quinazolinone derivatives (39) were reported as inhibitors of multi-pathways involved in cancer such as NF-kappaB, AP-1 mediated transcription and eIF-4E mediated translational activation\textsuperscript{74}.

Novel synthetic analogs of 5, 8-disubstituted quinazolines (40) blocked mitosis and induced apoptosis of tumor cells by inhibiting microtubule polymerization\textsuperscript{75}.

Some novel 2-thiophen-5-yl-3H-quinazolin-4-one (41) was synthesized and reported their analogs\textsuperscript{76} as inhibitors of transcriptional activation. A series of quinazolines linked pyrrolo [2,1-c][1,4]benzodiazepine (42) conjugates were prepared and screened for their anticancer activity\textsuperscript{77}.
Novel anticancer agents were prepared from 2-chloromethyl-4(3\(H\))-quinazolinone derivatives (43) with 4-anilinoquinazoline scaffolds\(^{78, 79}\). A novel 4-substituted quinazoline derivatives\(^{80}\) were synthesized and reported as DNA-gyrase
inhibitors. Synthesis and anticancer potential of 2-oxo/thioxooctahydro quinazolin-5-one derivatives and 4-amino-tetrahydro quinazolino [3,2-e]purine derivatives (44) were reported\textsuperscript{81,82}.

\[
\text{(43)}
\]

\[
\text{(44)}
\]

Discovery of \textit{N}-methyl-4-(4-methoxyanilino)quinazolines (45) as potent apoptosis inducers and the structure-activity relationship of the quinazoline ring were reported\textsuperscript{83}. Some novel [4,8-disubstituted-8,9-dihydro pyrazine quinazoline-7(6\textit{H})-ketones and a series of biquinazoline-2,2'-diones (46) were reported to possess antitumor activity\textsuperscript{84, 85}. Some of 4-anilino quinazoline derivatives, \textit{N}-alkyl(anilino) quinazoline derivatives, some 2,3-disubstituted quinazolin-4(3\textit{H})-ones and 4,6-disubstituted-1,2,3,4-tetrahydro quinazolin-2\textit{H}-ones (47, 48 and 49) were synthesized and reported to possess antitumor activity\textsuperscript{86-88}. 
Molecular docking for some novel quinazoline derivatives (50) were reported for their antitumor activity\textsuperscript{89}. Some new 2,6-substituted-quinazoline-4(3\(H\))-ones\textsuperscript{90} as non-classical antifolates were synthesized and evaluated for their biological action. A novel class of [4,8-disubstituted-8,9-dihydro pyrazine quinazoline-7(6\(H\))]-ketones\textsuperscript{91, 92} were reported as potential anti-cancer agents.

In 2011, some 2-halo-3-aryl-4(3\(H\))-quinazolinium halides\textsuperscript{93} and 2,3-disubstituted-8-arylamino-3\(H\)-imidazo quinazoline derivatives were synthesized and these compounds showed more potent antitumor activity. 2,4-diaminoquinazoline derivatives (51) were synthesized as protein 90 inhibitors\textsuperscript{94, 95}.

Li et al.,\textsuperscript{96} in 2011, synthesized 4-anilino quinazoline derivatives (52) and these compounds possessed epidermal growth factor receptor tyrosine kinase activity. Novel synthesized 6-fluoro-(3-fluorophenyl)-4-(3-methoxy anilino)quinazolines compound inhibited the insulin-like growth factor-I receptor produced anti-metastatic effect in human osteosarcoma U-2 OS cells\textsuperscript{97}. 
In 2011, a series of substituted quinazolines derivatives (53) and 3,5-diaryl isoxazoline/isoxazole linked 2,3-dihydro quinazolin-4-ones (54) were reported to possess antitumor activity\textsuperscript{98, 99}.
A series of novel 4-pyrrylamino quinazoline derivatives\textsuperscript{100} and 4,5-dihydro-1\textit{H}-pyrazolo[4,3-\textit{H}] quinazoline derivatives\textsuperscript{101} (55) were screened as potent kinase inhibitor. In 2011, some substituted furoquinazoline and quinoxaline derivatives\textsuperscript{102} (56) were reported to possess \textit{In-vitro} antitumor activity and some phenyl \textit{N}-mustard quinazoline conjugates were also evaluated for their antitumor activity\textsuperscript{103}.

Synthesis of non-classical quinazolinones (57) as \textit{thymidylate synthase} inhibitors and their evaluation of \textit{In-vitro} antitumor activity was reported\textsuperscript{104}. The compounds (57) were tested for the inhibition against bacterial (\textit{L. casei}) TS and/or human TS and for the cell growth inhibition of tumor cell lines of murine and human origin. The results indicated that most of the target compounds were generally potent inhibitors of \textit{L. casei} and human TS with IC\textsubscript{50} values of within the narrow range of 0.2-10 µM and 0.003-0.03 µM respectively.
Synthesis of series of 3-[5-amino-6-(2,3-dichloro phenyl)-[1,2,4]-triazin-3-yl]-6,8-dibromo-2-substituted quinazolin-4(3H)-ones\textsuperscript{105} (58) and their anticancer activity were reported. The compound 3-[5-amino-6-(2,3-dichlorophenyl)-[1,2,4]-triazin-3-yl]-6,8-dibromo-2-phenyl quinazolin-4(3H)-one was found to be most cytotoxic (CC\textsubscript{50}: 2.65 $\mu$g/ml) among the compounds tested.

\textit{In-vitro} antitumor activity of Novel quinazolin-4(3H)-ones derivatives with dithiocarbamate side chain\textsuperscript{106} (59) were synthesised and evaluated for their \textit{In-vitro} antitumor activity against human myelogenous leukemia K562 cells by MTT assay. The results of antitumor activity indicated that the entire compounds showed potent cytotoxicity and are more potent than the standard drug in inhibiting K562 cell growth with IC\textsubscript{50} values ranging from 0.5 to 31 $\mu$M.
A series of 5-(3’,4’,5’-substituted)-anilino-4-hydroxy-8-nitro quinazolines\textsuperscript{107} (60) were designed and synthesized to investigate the effect of the substitution on the inhibitory activity against mitotic progression of tumor cells. The effect of compounds on the proliferation of cell was evaluated using MTT assay and the results shown that compounds bearing an alkoxy substituent on the 5-anilino position having potent inhibition on the growth of HGC-27 cells at the concentration of 50 \(\mu\text{M}\).

![Chemical structures]

The phase-I and pharmacokinetic studies of halofuginone (61) in patients with advanced solid tumors were reported and the compound has entered into phase-II study\textsuperscript{108}.

![Chemical structure]

Synthesis, DHF reductase inhibition, antitumor testing and molecular modeling studies of some new quinazolin-4-(3\(H\))-ones (62) were reported\textsuperscript{109} and all the tested compounds exhibited antitumor activity with IC\textsubscript{50} values ranging from 0.4 to 70 \(\mu\text{M}\). Compound (63) exhibited more activity than other compounds.
2.4 ANTITUBERCULAR ACTIVITY

A series of quinazolines\textsuperscript{110} and quinazolinyl-4-thiazolidinone derivatives\textsuperscript{22} (64) were synthesized and its antitubercular activity was studied. The 4-thiazolidinone derivatives were screened at 12.5 µg/ml concentration against H\textsubscript{37}RV strain of \textit{M. tuberculosis} in BACTEC 12B medium using broth micro dilution assay and microplate alamar blue assay method. Some of the test compounds were found to be effective against \textit{M. tuberculosis} at this concentration.

The synthesis of 3-phenyl-6-methyl-4-(3\textit{H})-quinazolinone-2-yl-mercapto acetic acid arylidene hydrazide (65) and screening of synthesized compounds against \textit{M. tuberculosis} H\textsubscript{37}RV strain using BACTEC radiometric sensitivity test was reported\textsuperscript{111}.

The antitubercular activity of \textit{N}-3-(4-(4-chloro phenyl thiazol-2-yl)-(2-(amino)methyl)-quinazolin-4-(3\textit{H})-one} (66) and their derivatives was carried out against H\textsubscript{37}RV strain using L. J. medium\textsuperscript{112}. All the tested compounds exhibited antitubercular activity except \textit{p}-amino benzoic acid derivative.

The synthesis of manich base of 2-methyl quinazolin-4-(3\textit{H})-one\textsuperscript{113} (67) and their antitubercular activity evaluation against \textit{M. tuberculosis} H\textsubscript{37}RV strain using L. J.
medium at a concentration of 100, 10 and 1 µg/ml was reported. Out of four synthesized compounds, 6-chloro benzothiazole derivative showed complete growth inhibition at all tested concentration which is equivalent to standard streptomycin.

![Chemical Structure](image)

Some substituted furyl quinazolin-3(4H)-ones compounds exhibited potent antitubercular and anticancer activity\textsuperscript{114}. The synthesis of azetidine, quinazoline and triazolo thiadiazole containing pyrazine derivatives and their antimycobacterial activity was reported\textsuperscript{115}.

Some derivatives property\textsuperscript{116,117} of 2-phenyl-3-substituted quinazolin-4(3H)-one and 2-(5-aryl-1,3,4-oxadiazolyl)sulfanylacetamides was also showed antitubercular.

### 2.5 ANALGESIC AND ANTI-INFLAMMATORY ACTIVITY

A series of 4-phenyl-6,7,8,9-substituted-1,2,4-triazolo quinazolines\textsuperscript{118} (68), 1,5,7,8-tetrasubstituted-1,2,4-triazolo quinazolines\textsuperscript{119} (69) and a series of 2,6-
disubstituted quinazolin-4-ones\textsuperscript{120} (70) were reported to possess analgesic and anti-inflammatory activities.

![Chemical structures](image1)

Hardtman et al.,\textsuperscript{121, 122} synthesized some di and tri substituted 1,3,4-triazolo quinazolines (71, 72). These compounds exhibited anti-inflammatory, tranquillizing and antiviral activities.

A series of 1,2,8,9-tetra substituted-1,3,4-triazolo quinazolines\textsuperscript{123} (73) and substituted triazolo quinazolinones (74) were prepared and these compounds were found to exhibit antirheumatic activity.

The synthesis of some 1,5,7-trisubstituted-1,2,4-triazolo quinazolines\textsuperscript{124} (75) and 3-substituted aryl-2,6-disubstituted quinazolines\textsuperscript{125} (76) was reported and these compounds showed both analgesic and anti-inflammatory activities. In 1993, Srivastava et al.,\textsuperscript{126} prepared a series of substituted indolyl quinazolin-4-ones and studied their analgesic and anti-inflammatory activities.

A large number of new ethyl-1-methyl-5-[4-oxo-3(4\textsubscript{H})-quinazolinyl]-1\textsubscript{H}-pyrazole-4-acetates\textsuperscript{127} (77) were prepared and its analgesic activity was evaluated. Among these, compounds bearing 2-methyl, 2-ethyl and 2-phenyl moiety substituted at the 2\textsuperscript{nd} position of the quinazolinone ring proved to be more active than acetyl salicylic acid and phenylbutazone in the phenyl benzoquinone writhing test.
Some 6-substituted-2-alkyl-3-(4-amino benzene sulphonamido) quinazolin-4-ones\textsuperscript{128} (78) and a series substituted quinazolines\textsuperscript{129} (79) were synthesized and reported that they possessed anti-inflammatory activity.

![Chemical structure](image1)

In 1998, 2,3-disubstituted-6-bromo quinazolin-4-ones\textsuperscript{130} (80) and certain analogs of 2-methyl-3-substituted quinazolin-4-ones\textsuperscript{131} (81) were reported for their anti-inflammatory activity. Some novel benzopyrazolyl, benoxazolyl, quinazolinyl derivatives of quinazolin-4-ones were prepared and tested them for their anti-inflammatory activity\textsuperscript{132-134}.

![Chemical structure](image2)

New isatin hydrazones (82) containing different heteroaryl group such as 2-substituted quinazoliny1 acetic acid hydrazide and benoxazinony1 acetic acid hydrazide were prepared\textsuperscript{135} and their analgesic activity were assayed by acetic acid induced writhing method. Among these, compound 7-methyl isatin-3-\textsuperscript{1}\textsuperscript{N-2-\textsuperscript{2}(2-phenyl-3,4-dihydro-4-oxo-quinazolin)-3-methyl carbonyl]-hydrazone was the potent compound of this series.
The synthesis of some 3-substituted quinazolin-4-ones\textsuperscript{136} (83) and a series of 3-(thiadiazolylamino)-2,6,8-trisubstituted quinazolin-4-ones\textsuperscript{137} (84) were reported for their anti-inflammatory activity.

A series of 1,2,4-triazolo[4,3-c]quinazolines\textsuperscript{138} (85) were evaluated for their CNS activities and these compounds showed both analgesic and anticonvulsant activities.

The properties of 6,7,8-unsubstituted quinazolinone was improved by substituting groups that have similar lipophillic character but exert opposite electronic effects on the quinazoline nucleus\textsuperscript{139} (86). The pharmacological data obtained for these compounds (86) were compared with previously reported unsubstituted analogs compound, it seems that 6-Cl, 7-Cl and 8-CH\textsubscript{3} substitution on quinazolinone does not generally show any advantage for the analgesic activity. The potent compound of this
series was found to be ethyl 2-(5-(7-chloro-4-oxo-2-phenyl quinazolin-3(4H)-yl)-1-methyl-1H-pyrazol-4-yl)-acetate.

![Image of compound 86](image)

Alagarsamy et al., synthesized some novel 1-[2-phenyl quinazolin-3-yl-4(3H)-one]-3-(substituted)-thiourea (87) and a series of substituted quinazolin-4(3H)-ones by replacing the phenyl group with methyl group at 2\textsuperscript{nd} position (88) and evaluated their analgesic and antiinflammatory activity. Biological evaluation of these compounds exhibited more significant analgesic and anti-inflammatory activities than the phenyl substituted series.

![Image of compounds 87 and 88](image)

A series of 2-benzylamino-3-(substituted)-quinazolin-4-(3H)-ones (89) by incorporating the benzylamino group instead of phenyl group at 2\textsuperscript{nd} position of quinazolinones were synthesized and among them the compound 2-{(benzylamino)-3-(3-phenyl allylideneamino)-quinazolin-4(3H)-one was found to be the most active analgesic agent and it was equipotent with standard diclofenac sodium.
The synthesis of novel quinazolinone derivatives\textsuperscript{143} (90) and their evaluation of analgesic activity was reported. The report showed that 2-[(ω-chloro acetonyl)-3-substituted phenyl-6-halo/6,8-dihalo quinazolin-4-(3\textit{H})-ones exhibited mild to moderate activity at a dose of 50 mg/kg p.o. Whereas 2-[(ω-hydrazino acetonyl)-3-substituted phenyl-6-halo/6,8-dihalo quinazolin-4-(3\textit{H})-ones (91) exhibited poor activity. However the pyrazoline derivatives of parent compound (92) exhibited more potent activity than (90) and (91).

Some new 2,3,6-trisubstituted quinazolinones\textsuperscript{144} were synthesized by introducing 2-substituted indol-3'-yl moiety at 3\textsuperscript{rd} position and substituted phenylamino acetyl methylene chain at 2\textsuperscript{nd} position of quinazolinone. Analgesic activity was performed by acetic acid induced writhing test in mice at a dose of 50 mg/kg p.o. Compound (93) exhibited mild to moderate analgesic activity. Furthermore, cyclisation of (93) into their corresponding compound (94) results in increased activity.
The synthesis of novel 2-methyl quinazolin-4-(3H)-ones\textsuperscript{145} (95) were synthesized and evaluated for their analgesic activity by tail-immersion method in mice. The entire
synthesized compounds (95) exhibited only mild analgesic activity compared to the standard pentazocine.

A series of 1-[2-methyl thio quinazolin-3-yl]-4(3H)-one]-3-(substituted) thiourea\textsuperscript{146} (96) were prepared and the compound 1-[2-methylythio quinazolin-3-yl]-4(3H)-one]-3-diethyl thiourea was exhibited more activity than standard diclofenac sodium. By using isosteric principle, some novel 2-mercapto-3-(substitutedamino)-5,6,7,8-tetrahydro-3H-benzo[4,5]-thieno(2,3-d)-pyrimidin-4-ones\textsuperscript{147} (97) was prepared and evaluated for its analgesic activity [thienopyrimidine is bioisostere of quinazoline].

![Chemical structures](image)

Studies on anti-inflammatory activity of some biologically active 6,8-disubstituted-2-phenyl-3-[substituted-benzothiazol-2-yl]-4(3H)-quinazolinones\textsuperscript{148} (98 and 99) indicated that all the test compounds are less potent than standard drug.

![Chemical structures](image)

Some synthesized novel quinazolinones\textsuperscript{149} (100) were exhibited good anti-inflammatory activity ranging from 62.2 to 80.7% reduction in edema volume compared to standard ibuprofen.
The effect of incorporating thiazolidinone and azetidinone on anti-inflammatory activity of novel quinazolin-4-(3H)-ones was studied using carrageenan induced paw edema method in rats. All the compounds (101 and 102) exhibited anti-inflammatory activity of varying degree from 16.3 to 36.3%.

Analgesic activity of 3-[4′-(p-chlorophenyl)-thiazol-2′-yl]-2-[(substitutedazetidinone/thiazolidinone)-aminomethyl]-6-bromo quinazolin-4-ones was studied using acetic acid induced writhing test on mice. All the synthesized compounds (103) exhibited mild analgesic activity.
Some substituted quinazolinones\textsuperscript{152} (104) were synthesized and evaluated for their analgesic activity by acetic acid induced writhing method. The analgesic data of this study indicated that the entire derivatives exhibited only mild to moderate activity and the introduction of 2'-aminophenyl at N-1 of quinazolinone does not increase the activity.

Synthesis of some 3-(4-methyl phenyl)-2-substituted amino quinazolin-4(3\textit{H})-ones\textsuperscript{153} (105), series of 3-(4-ethyl phenyl)-2-substituted amino quinazolin-4(3\textit{H})-ones\textsuperscript{154} (106) and some 3-(2-pyridyl)-2-substituted quinazolin-4(3\textit{H})-ones\textsuperscript{155} (107) and evaluation of their analgesic and anti-inflammatory activities were reported.

Some 3-cyclohexyl-2-substituted hydrazino quinazolin-4(3\textit{H})-ones\textsuperscript{156} (108) and a series of 3-(3-ethyl phenyl)-2-substituted hydrazino-3\textit{H}-quinazolin-4-one derivatives\textsuperscript{23} (109) were prepared and studied for their analgesic and anti-inflammatory activities.
Some novel 2-(2,4-disubstituted-thiazole-5-yl)-3-aryl-3H-quinazoline-4-one derivatives\(^{157}\) (110) were prepared and screened for their anti-inflammatory activity. In 2009, some azolopyrimidoquinolines, pyrimido quinazolines\(^{158}\) (111 and 112) were synthesized and reported that these compounds possessing anti-oxidant, anti-inflammatory and analgesic activities.
A series of novel 2-thiophen-5-yl-3H-quinazolin-4-one analogs\textsuperscript{159} were synthesized and reported that these compounds possess anti-inflammatory and anti-cancer activities.

Novel quinazoline derivatives\textsuperscript{160} (113) and novel 6,7,8,9-tetrahydro-5H-5-hydroxyphenyl-2-benzylidin-3-substituted hydrazino thiazolo(2,3-b) quinazolines\textsuperscript{161} were synthesized and evaluated for their analgesic and anti-inflammatory activities. A series of 6-bromo-2-phenyl-3-substituted-4-quinazolinone derivatives\textsuperscript{162} (114) were synthesized and studied their anti-inflammatory, analgesic and antibacterial activities.

Some 2,3-dihydro quinazolin-4(1H)-one derivatives\textsuperscript{163}, some 3-aryl-2-substituted-1,2-dihydro quinazolin-4(3H)-one derivatives\textsuperscript{164} and some novel 2-substituted-quinazolin-4(3H)-ones\textsuperscript{165} were synthesized and screened for their analgesic and anti-inflammatory activities.
In 2010, series of spiro[2H, 3H] quinazoline-2,1’-cyclohexan]-4(1H)-one derivatives were prepared and applied for docking studies. These compounds exhibited anti-inflammatory and analgesic activities.\(^{166}\)

Some of new 2,3-disubstituted-1,2-dihydro quinazolin-4(3H)-one derivatives\(^ {167}\) and some novel 6,8-dibromo-4(3H)-quinazolinone derivatives\(^ {168}\) were prepared and studied their anti-inflammatory and analgesic activities.

In 2011, a series of quinazolin-4(1H)-one derivatives\(^ {169}\) were prepared and studied their anti-inflammatory and analgesic activity.

### 2.6 Antiviral Activity

Anti-HIV activities of some novel 2,3-disubstituted quinazolin-4(3H)-ones \(^ {115}\) were reported by Alagarsamy\(^ {170}\) et al. Compound 2-mercapto-3-[(benzimidazol-1-yl)-methylamino]-quinazolin-4-(3H)-one and 2-mercapto-3-[(aniline-N-yl)-methylamino]-quinazolin-4-(3H)-one exhibited maximum 31% and 25% protection respectively against HIV-1. Whereas, 2-mercapto-3-[(pyridine-2-yl)-methylamino]-quinazolin-4-(3H)-one showed 27% protection against HIV-2.

Thiadiazolyl quinazolones\(^ {171}\) \(^ {116}\) were synthesized as potential antiviral agents and these compounds were evaluated against Japanese Encephalitis Virus (JEV) and Herpes Simplex Virus-1 (HSV-1). Compounds containing \(R = \text{n-propyl}\) was found to more active against JEV.
In 2005, synthesis and anti-HIV studies of 3-[5-amino-6-(2,3-dichloro phenyl)-1,2,4-triazin-3-yl]-6,8-dibromo-2-substituted-quinazolin-4(3H)-ones\textsuperscript{172} \textbf{(117)} were reported and the results revealed that none of the test compounds exhibited anti-HIV activity; whereas, entire test compounds displayed cytotoxic properties in MT-4 cells.

A series of 1,3,4-trisubstituted pyrrolidines\textsuperscript{173} were discovered and studied the effect of fused heterocyclics on antiviral activity and pharmacokinetic properties. Imidazopyridine derivative showed eight fold more potency than its regioisomer. Incorporation of carbonyl group into benzimidazole derivative resulted in the formation of quinazolinone compounds \textbf{(118)}. But this compound exhibited very less activity than benzimidazole derivative.
Isoquinolinyl quinazolines\textsuperscript{174} (119) were synthesized and its antiviral activity was tested against Influenza virus in embryonated hen’s egg at the concentration of 0.5 mg and these compounds showed varying degree of antiviral activity.

In 2006, 1,3,5-\textit{tri}-\textit{p}-\textit{[}(2-aryl-3\textit{H}-quinazolin-4-one-3-yl)-phenyl]-2,4,6-hexahydro-1,3,5-s-triazines (120) were synthesized as potential anti- Tobacco Mosaic Virus (TMV) agents\textsuperscript{175} and four title compounds were screened for their antiviral activity against TMV. All the title compounds were found to be active against TMV.

Synthesized quinazolinyl syndones\textsuperscript{176} (121) were evaluated for their \textit{in vitro} antiviral activity against JEV and HSV-1 and the tested compounds with phenyl and styryl substituent showed similar degree of effect for anti-HSV-1 activity.
Antiviral activity of oxo/thiono triazolo isoquinolinyl quinazolones\textsuperscript{(122)} was studied against Influenza virus. The results showed that test compounds exhibited varying order of antiviral activity.

![Chemical Structures](https://example.com/chemical_structures)

Synthesis of some amino acids incorporated quinazolin-4-(3H)-one \textsuperscript{(123)} as possible antiherpes viral agents were reported\textsuperscript{(178)}. These compound were tested for \textit{in vitro} antiviral activity against Herpes Simplex Virus type-1 (HSV-1) using CPE inhibition assay. Among the test compounds, proline derivative showed good protection till 72 h at the concentration of 300 and 400 µg/ml.
Synthesis and antiviral activity of 2-aryl/methyl-3-(substituted benzylamino)-quinazolin-4-(3H)-ones (124) were reported\textsuperscript{179}. The compound having $R_1=4\text{-CF}_3$ showed curative rates of 55% which was slightly higher than that of reference (54%) against TMV at 500 µg/ml concentration.

\[
\begin{align*}
\text{(123)} & \quad \text{(124)}
\end{align*}
\]

In 2010, Schiff bases of some 2-phenyl quinazoline-4(3H)-ones\textsuperscript{180} were synthesized and evaluated for their antiviral activity and cytotoxicity. Novel series of 2,4-diaryl-4,6,7,8-tetrahydro quinazolin-5(1H)-one\textsuperscript{181} derivatives were synthesized as anti-HBV agents.

In 2011, a series of 2-phenyl-3-substituted quinazoline-4-(3H)-ones\textsuperscript{182, 183} were synthesized and these compounds screened for their antiviral and cytotoxic activities.

2.7 CNS ACTIVITY

Some 2-methyl-3-(o-tolyl) quinazolin-4(3H)-ones and 2-methyl-3-(o-chlorophenyl) quinazolin-4(3H)-ones\textsuperscript{24} (125) was prepared and these compounds were reported to possess sedative, hypnotic and anticonvulsant activities. Some 3-(substituted phenyl)-2-substitutedmethyl-4-oxo quinazolines\textsuperscript{184} (126) was also synthesized and studied their antiparkinsonism activity.

\[
\begin{align*}
\text{(125)} & \quad \text{(126)}
\end{align*}
\]
A series of 3-(2-benzthiazolyl)-2,6-disubstituted quinazolin-4(3H)-ones\textsuperscript{185} (127), some 2-fluoromethyl-3-substituted phenyl-6-amino quinazolin-4(3H)-ones\textsuperscript{186} (128) and Certain analogs of 2-substituted thio-3-substituted phenyl quinazolin-4-(3H)-ones (129) with chloro group at C–7 position\textsuperscript{187} were exhibited CNS depressant activity.

A series of 2-(((5-ethyl-5-phenyl-1-barbituryl) methyl) carbonyl) thio-3,6,8-trisubstituted quinazolin-4(3H)-ones\textsuperscript{188} (130) and a series of 3-substituted-6,8-dichloro-2-phenyl-4(3H)-quinazolines\textsuperscript{189} (131) were prepared and these compounds were reported to possess good anticonvulsant activity.

Some 1,3-disubstituted quinazolin-2,4-diones\textsuperscript{190} (132), some acetylenic quinazoline derivatives\textsuperscript{191} and a series of 7,8-methylenedioxy-4H-2,3-benzodiazepin-4-ones (a) and 6,7-methylenedioxy phthalazin-1-(2H)-ones\textsuperscript{192} (133) were synthesized and
screened for their anticonvulsant activity. The tested compounds were showed good anticonvulsant property.

In 2004, in order to develop more potent anticonvulsant agents with minimum or no side effects, a series of compounds having two heterocyclic moieties such as quinazolinone and 2-oxo/thiobarbituric acid into a single molecular frame work were synthesized. The 3-(amino ethyl ethanoate)-2-methyl-6-mon/6,8-dihalo substituted quinazolin-4-(3H)-ones (134) exhibited less anticonvulsant activity in MES and PTZ induced seizures. Whereas thiosemicarbazide of 1-[3-substituted-2’-methyl-6’-mono/6’,8’-dihalo substituted quinazolin-4’-(3’H)-ones (135) exhibited more anticonvulsant activity in MES and PTZ induced seizures. 

\[
\text{R} \quad \text{R}_1 \\
\text{132}
\]

\[
\text{X} \quad \text{R} \\
\text{133}
\]

\[
\text{NHCH}_2\text{COOC}_2\text{H}_5 \\
\text{NHCH}_2\text{CONHNHCNH}_2 \\
\text{134}
\]

\[
\text{135}
\]

In 2005, synthesis and isolation of new regioisomeric 4-thiazolidinones (136, 137) and their anticonvulsant activity was reported. Among the synthesized compounds, selected members of thiazolidinone were screened and found to possess moderate anticonvulsant activity.
Synthesis and anticonvulsant activity of some substituted benzothiazole derivatives of thioquinazolinone \((138)\) was reported\(^ {195}\). The iodo derivatives were shown more activity than bromo derivatives.

The synthesis and anticonvulsant activity of some novel 3-[5-substituted-1,3,4-thiadiazol-2-yl]-2-styryl quinazolin-4(3H)-ones\(^ {196}\) \((139)\) was reported. Out of synthesized compounds, only six compounds were found to exhibit anticonvulsant activity in MES method. While some of these compounds exhibited better sedative-hypnotic activity and CNS depressant activities.
In 2010, some novel 3-[[substituted]-amino]-2-2-phenyl-3H-quinazolin-4-ones\textsuperscript{197} was prepared and studied their anticonvulsant and neurotoxicity effects.

Some new spiro-derivatives of benzo[H] quinazolines\textsuperscript{198} were synthesized and these derivatives found to possess antineoplastic and anti monoamino oxidase activities.

In 2011, some novel 6,7,8,9-tetra hydro-5H-5-(2'-hydroxy phenyl)-2-(4'-substituted benzylidene)-3-(4-nitro phenylamino) thiazolo quinazoline derivatives\textsuperscript{199} and a novel 2-(substituted)-3-[[substituted]amino]quinazoline-4(3H)-ones\textsuperscript{200} (140) were synthesized and evaluated for their anticonvulsant activity.

![Chemical Structure](image)

(140)

**2.8 ANTIMICROBIAL ACTIVITY**

The significant antibacterial and antifungal activity was showed by some 2,3-disubstituted quinazolin-4(3H)-ones\textsuperscript{201,202} (141, 142) and a series of 1,2,4-triazolo quinazolines\textsuperscript{25} (143).

A series of 2-substituted quinazolines\textsuperscript{203} bearing a thiophene ring at 3rd position (144) were found to exhibit significant antifungal activity. A series of 2-oxatriazolin-4(3H)-quinazolines\textsuperscript{204} (145) were reported to possess antimicrobial activity.
A series of 3-aryl-2-pyridinium ethyl-4(3H)-quinazolines\textsuperscript{205}, 2-guanidino-3-substituted quinazolin-4-ones\textsuperscript{206} (146) and 2-morpholino-6-chloro-4-substituted quinazolines\textsuperscript{207} (147) were prepared and reported that these compounds were found to exhibit antibacterial activity.

In 1995, the synthesis of a series of 2,4-diamino-6-methylamino quinazolines\textsuperscript{208} (148) and its derivatives was reported. These compounds were found to exhibit antifungal activity. A series of 2,4-diamino quinazolines\textsuperscript{209} (149) by replacing the 6-methylamino group with the thiophenyl group was reported and these compounds were found to exhibit selective inhibition of \textit{Candida albicans} dihydrofolate reductase.
A series of 2,4-diamino quinazolines\textsuperscript{210} (150) by introducing halogen at 5\textsuperscript{th} and 6\textsuperscript{th} position and some novel 2-substitutedmethyl-3-(4-substitutedsulphonamido phenyl) quinazolin-4(3H)-ones\textsuperscript{211} (151) were synthesized and these compounds showed significant antibacterial activity. Some imidazolo quinazolines and 3-substituted quinazolin-4-ones\textsuperscript{212} (152) were prepared and the biological investigation of these compounds showed efficient antifungal activity.

In 1997, some 2-benzyl-3-aryl quinazolin-4-ones\textsuperscript{213} (153), certain analogs of 2-phenyl-3-substituted quinazolin-4(3H)-ones\textsuperscript{214} (154), a series of 2,3-disubstituted quinazolines\textsuperscript{215} (155) and some novel substituted bisquinazolin-4-ones\textsuperscript{216} (156) were reported that these compounds were able to exhibit antimicrobial activity.
The synthesis and antifungal activity of a series of 2,6,8-trisubstituted-3-(2-thiazolyl) quinazolin-4-ones\textsuperscript{217} (157) and some 2-substituted aryl-6,8-disubstituted quinazolin-4-ones\textsuperscript{218} were reported.

In 1997, the synthesis of some novel 2,6,8-trisubstituted quinazolines\textsuperscript{219} and certain analogs of 2-phenyl-6-iodo quinazolin-4(3\(H\))-ones\textsuperscript{220} were studied for their antimicrobial activity.
In 1998, some novel 2,3-disubstituted quinazolines\textsuperscript{221} (158), a series of 2-(nitrofurylvinyl)-3-substituted arylquinazolines\textsuperscript{222} (159), a series of 1-methyl-2-thioxo-3-substituted quinazolin-4-ones\textsuperscript{223} (160) and certain analogs of 2-methyl-3-substituted quinazolines\textsuperscript{224} (161) were synthesized and these compounds were reported to possess antimicrobial activity.

A series of 2-ethyl-6-iodo-3-substituted quinazolines\textsuperscript{225} (162) were prepared and these compounds were exhibited antibacterial activity.

The synthesis of several 2,3-disubstituted quinazolin-4-ones\textsuperscript{226}, 2-methylbenzylamino quinazolin-4(3H)-ones\textsuperscript{227} and 1-(2-methyl-4-quinolinyl) quinazolin-
2-ones were reported that these compounds were able to inhibit the growth of various microorganisms.

A series of novel 6,8-disubstituted-2-aryl quinazolin-4(3H)-ones and certain analogs of 3-aryl-2-(4-arylthiazol-2-yl-amino methyl) quinazolin-4-ones were synthesized and these compounds were reported to possess antifungal activity.

Various 2,3-disubstituted quinazolin-4-one derivatives by introducing the chloro group at 6th and 8th positions and some 2,3,6,8-tetrasubstituted quinazolin-4(3H)-ones were reported to have an antimicrobial activity.

A series of 2-furyl vinyl-3-aryl quinazolin-4(3H)-ones and some novel oxoquinazolyl thiosemicarbazones were synthesized and these compounds were exhibited antibacterial activity.

Preparation of series of N,N-disubstituted dithiocarbamic esters derived from 2-methyl quinazolines were reported and these compounds were found to possess antifungal activity. The structural activity relationship of a series of 2-substituted quinazolines and their antibacterial activity were reported in the year 1999.

A series of substituted quinazolines were reported and studied their antimicrobial activity.
Some Schiff’s and Mannich bases of isatin derivatives with 3-amino-2-methylthio quinazolin-4(3H)-ones\(^\text{238}\) were synthesized and reported for their antibacterial, antifungal and anti HIV activities.

The synthesis of some novel hydroxamic (4-quinazolinyl) thioesters\(^\text{239}\) was reported and these compounds were found to exhibit antifungal activity. A series of 3-amino-2-substituted quinazolin-4-ones\(^\text{240}\) (169) were synthesized and studied for their antiviral activity.

Some new fluorinated hydroquinazoline derivatives\(^\text{241}\) (170) were prepared and studied for their antifungal activity. Synthesized imidazo[2',1':5,1]-1,2,4-triazolo[4,3-c]-quinazoline derivatives of 5-thioxo-1,2,4-triazole, 4-oxothiazolidine, and their open-chain counterparts were evaluated for their antibacterial activity\(^\text{242}\).
The synthesis and evaluation of new quinazolone (171) derivatives of nalidixic acid as potential antibacterial and antifungal agents were reported. Some of the derivatives showed marked inhibitory activity against enteric pathogen like aeromonas hydrophila, a causative agent of diarrhoea in both children as well as adults.243

In 2006, synthesis of 6-ido/bromo-3-amino-2-methylquinazolin-4(3H)-ones (172) by direct halogenations and their schiff base derivatives were reported.244 All the
compounds exhibited a marked degree of activity against bacteria in comparison to tetracycline.

The new 2,3-disubstituted quinazolin-4(3H)-ones\textsuperscript{245} (173) as antimicrobial agents were reported. The overall screening result showed that the compounds containing chloro and methoxy group displayed significant antibacterial activity at 100 µg/ml and 200 µg/ml. Some novel substituted 2-imidazolyl-N-(4-oxo-quinazolin-3(4H)-yl)-acetamides\textsuperscript{246} (174) were synthesized and screened for antimicrobial activity.

In 2009, ([1,2,4]Triazolo[1,5-c]quinazolin-2-yl-thio)carboxylic acid amides\textsuperscript{247} was synthesized and these compounds showed cytotoxicity by bioluminescence inhibition, antibacterial and antifungal activity.

Synthesis of 2-thio-[1,2,4]triazolo[1,5-c]quinazoline derivatives were exhibited good antimicrobial activity\textsuperscript{248}.

\[ \text{Figure 172} \]

\[ \text{Figure 173} \]

\[ \text{Figure 174} \]
In 2009, some novel quinazolinones fused with [1,2,4]-triazole, [1,2,4]-triazine and [1,2,4,5]-tetrazine rings (175a,b,c) were synthesized and have been demonstrated their antibacterial activity against gram-negative bacteria, *Escherichia coli*, *Pseudomonas aeruginosa* and gram-positive bacteria, *Streptococcus pneumoniae*, *Bacillus subtilis*, as well as demonstrated significant antifungal activity against fungi *Candida albicans*, *Aspergillus fumigatus*, *Aspergillus flavus*, and *Aspergillus niger*. The studies documented that the presence of triazole ring exhibited greater activity than that of triazine and tetrazine.

A 3-amino-6, 8-dibromo-2-phenylquinazolin-4(3H)-ones (176) was prepared and these compounds showed anti-microbial activity.
A series of ethoxy phthalimide derivatives of tetrahydro-naphtho[1,2-e][1,5]benzo diazepine and dihydrobenzo[H] quinazolines\textsuperscript{251} (177) were screened for their antimicrobial activity. In 2009, the antimicrobial activity of newly synthesized 6-substituted indolo[1,2-c]quinazolines\textsuperscript{252} (178) were documented.

In 2010, synthesized novel 4-substituted quinazoline derivatives evaluated for their antimicrobial activity and docking studies of these compounds as DNA-gyrase inhibitors\textsuperscript{253} were also done.

In 2010, mannich bases of benzimidazo [1,2-c] quinazolin- 6(5H)-thione\textsuperscript{254}, some of new non-classical acridines, quinolines and quinazolines derived from dimedone\textsuperscript{255} and some (4-oxo-thiazolidinyl) sulfonamides bearing quinazolin-4(3H)-ones\textsuperscript{256} were evaluated for their antimicrobial activity.

The novel 6,8-dibromo-4(3H) quinazolinone derivatives\textsuperscript{257} were reported as antibacterial and antifungal agents. Some 2,3-disubstituted quinazolin-4(3H)-ones were synthesized and studied for their antileishmanial and antimicrobial activity\textsuperscript{258}.

In 2010, a series of novel 3-(5-amino-6(2,3-dichlorophenyl)-1,2,4-triazin-3-yl)-2-aryl quinazoline-4(3H)-ones\textsuperscript{259} (179) were prepared and these compounds showed in vitro antibacterial activity.

Synthesized compounds of some pyrazolo-3-aryl-4(3H)-quinazolinones derivatives \textsuperscript{(180)} and a series of novel 5-amino-4-cyano-1H-pyrazole and quinazolin-
4(3\textit{H})-one derivative were screened for antimicrobial activity and these compounds were found to be more potent antimicrobial agents\textsuperscript{260, 261}.

![Chemical structures](179.png)

![Chemical structures](180.png)

In 2011, a series of urea/thiourea derivatives of quinazolinone-lysine conjugates (181a & 181b) and pleuromutilin derivatives with quinazolinone and thioether groups were studied for their antimicrobial activity\textsuperscript{262, 263}. New 1,3-oxazolyl-7-chloro quinazolin-4(3\textit{H})-ones\textsuperscript{264} and 4(3\textit{H})-quinazolinones\textsuperscript{265} (182) were synthesized and evaluated for their antimicrobial activity.

In 2011, some 3-[benzimidazo-benzothiadiazoleimidazo-[1,2-c]quinazolin-5-yl]-2\textit{H}-chromene-2-ones\textsuperscript{266} (183a & 183b) were prepared and documented as potent antimicrobial agents.
2.9 MISCELLANEOUS ACTIVITY

In 1988, some substituted-1,3,4-triazolo quinazolines\textsuperscript{267} (184) were synthesized and these compounds were found to possess significant adenosine antagonistic activity.

In 1991, a series of novel [1,2,4]triazolo[1,5-c]quinazolin-5(6H)-ones\textsuperscript{268} were synthesized and reported their binding affinity towards benzodiazepine receptor.
A series of 4-(substituted benzylamino)-6,7,8-trimethoxy quinazolines\textsuperscript{269} (185) and 2-(pyridyl/imidazolyl)-4-(substituted anilino) quinazolines\textsuperscript{270} (186) were synthesized and biological investigation of these compounds showed good cGMP-PDE inhibition activity.

Some substituted-1,2,4-triazolo quinazolines\textsuperscript{271} (187) and 1,2,3-triazolo[1,5-a]quinazolines\textsuperscript{272} were prepared and these compounds were reported to possess affinity towards adenosine and benzodiazepine receptors.

In 1995, some 2-substituted-4-(substituted anilino) quinazolines\textsuperscript{273} (188) were prepared and studied for their affinity towards nerve growth factor.

The synthesis of some 3,5,6,7,8-substituted quinazolin-2,4-diones\textsuperscript{274} (189) and certain analogs of 3-(2-mercapto ethyl) quinazolin-2,4-diones\textsuperscript{275} (190) were reported.

Some 4-substituted anilino quinazolines\textsuperscript{276} (191) were synthesized and studied for their enzyme inhibition activity. These compounds were reported to possess
significant tyrosine kinase inhibition activity. The selectivity of derivatives of the triazoloquinazoline adenosine antagonist\(^{277}\) towards human A3 receptor subtype was reported.

A series of 4-substituted anilino quinazolines\(^{278}\) with substitution at 3\(^{rd}\) position (192) and at 7\(^{th}\) and 8\(^{th}\) positions\(^{279}\) (193) were synthesized and these compounds were found to possess good tyrosine kinase inhibition activity.

Some 2,3-disubstituted quinozoin-4(3\(H\))-ones\(^{280}\) were synthesised and these compounds exhibited the AMPA receptor antagonistic activity. In 1997, 4-aryl-1,2,3,4,5,6,7,8-octahydroquinazolin-2-thione derivatives\(^{281}\), certain analogs of 1-(2-carboxy ethyl) quinazolin-2,4-diones\(^{282}\), fused heterocyclic quinazolin-4(3\(H\))-ones\(^{283}\) and 2,3-disubstituted quinazolin-4(3\(H\))-ones\(^{284}\) were synthesized and reported for their biological activities.

Some non-classical 2-amino-5,7-disubstituted tetrahydro quinazolin-4-ones\(^{285}\) (194) were synthesized and studied for their thymidylate synthetase inhibition activity.
In 1997, synthesis of condensed quinazolines from 3-aryl-4-quinazolones\textsuperscript{286} and substituted quinazolin-4(3\textit{H})-ones\textsuperscript{287} (195) were reported.

Some 4-(anilino), 4-(phenoxy), 4-(thiophenoxy)-6,7-dimethoxy quinazolines\textsuperscript{288} (196), imidazo[3,4-\textit{a}] quinazolinones\textsuperscript{289} (197), 6-substituted-2-cyano methyl quinazolin-4(3\textit{H})-ones\textsuperscript{290} (198) and a series of 1,2,4-triazolo quinazolines\textsuperscript{291} (199) were synthesized and reported in the year 1997.

In 1998, some substituted-1,3,4-triazoloquinazolines\textsuperscript{292} (200) and a series of 3-phenyl-2,6-disubstituted quinazolin-4(3\textit{H})-ones\textsuperscript{293} (201) were prepared and these compounds were found to exhibit adenosine antagonistic activity.
Synthesis of some 2,4,8-trisubstituted quinazolines (202), 2,3-disubstituted-1,2,3,4-tetrahydro quinazolin-4-ones (203), novel spirothiazolidinone and spiroazitidinone derivatives incorporated with quinazolines and a series of 5-substituted quinazoline derivatives were reported.

In 1998, synthesis of some 1,2,4-triazino[4,3-c] quinazolines and 4-(pyrazol-1-yl) quinazolines, 3-substituted-2-phenylamino-4-oxo quinazolines, spiroquinazoline-4-heterocyclic derivatives, some novel 2-substituted-3-aryl quinazolin-4(3H)-ones from 2-cyano methyl-3-substituted phenyl-4(3H)-quinazolinone, some 3-acetoxy amino quinazolin-4(3H)-ones, certain analogs of 4-substituted arylamino quinazolines from 2-amino-N-arylbenzamidines, 2-cyano-4-alkoxy-6,7-dimethoxy quinazolines and certain analogs of 2,4-diamino quinazolinones, some 4-quinazolinone oxime ethers (208) were reported.
Some 2,3-disubstituted quinazolin-4(3H)-ones\textsuperscript{307} (209) were synthesized and studied for their mono amino oxidase inhibition activity.

![Chemical Structures](image)

In the same year synthesis of cyclohexylidene hydrazide derivatives of 3-phenyl-4(3H)-quinazolinones\textsuperscript{308} (210), condensed quinazoline thiones\textsuperscript{309} (211), certain analogs of 5,6,7,8-tetrahydro quinazolines\textsuperscript{310}, some 2-(trifluoromethyl)-3-substituted-4-oxo quinazolines\textsuperscript{311} (212) from 3-amino-2-(trifluoro methyl) quinazoline, substituted benzimidazolo, triazolo, tetrazolo and thia diazolo quinazolines\textsuperscript{312} and some 3-substituted amino-2-methyl-4-oxo quinazolines\textsuperscript{313} (213) were also reported. Some 2-
(substituted amino)-3-(alkoxyl phenyl) quinazolin-4(3H)-ones (214) were showed oestrogen agonistic activity\textsuperscript{314}. A series of 3-(substituted methyl)-2,6-disubstituted quinazolin-4(3H)-ones (215) were found to exhibit good antiamoebic activity\textsuperscript{315}.

Mateo et al.,\textsuperscript{316} described the intramolecular aza-witting reaction of imino-phosphoranes with β-lactam carbonyl group of substituted quinazolin-4-ones. The microwave promoted synthesis of substituted quinazolin-4-(3H)-ones\textsuperscript{317} was reported in 1999.
Various groups described the synthetic approaches for the fused heterocyclo quinazolones\textsuperscript{(216)}, 2-substituted quinazolinones\textsuperscript{(217)}, some novel substituted quinazolin-4-ones\textsuperscript{(218)} and 2-substituted quinazolin-4(3H)-ones\textsuperscript{(219)}.

In 1999, synthesis of a series of oxindole quinazolines\textsuperscript{(220)}, some substituted pyrido quinazolines\textsuperscript{(221)} (218), some novel benzimidazo[1,2-c] quinazolin-6(5H)-ones\textsuperscript{(222)} (219) and 6-substituted benzimidazo[1,2-c]quinazolines\textsuperscript{(223)} were documented.

Ji Wang et al.,\textsuperscript{(224)} described the synthesis of 3-(substituted biphenyl)-2-substituted quinazolin-4(3H)-ones (220) and these compounds showed angiotensin-II antagonistic activity.
The synthesis and bronchodilator activity of 7,8,9,10-tetrahydroazepino[2,1-b]quinazolines were reported in the year 1999. In the same year, the synthesis of some 2-morpholino methyl-3-substituted quinazolin-4(3H)-ones, 2-phenyl-3-substituted-4-oxo quinazolines (221), 3-(6-amino-2-pyridyl)-2-methyl-4(3H)-quinazolinone (223) and 2-substituted quinazolin-4(3H)-ones (224) were also described with their chemical reactions.

In 2000, substituted 1,2,3-triazolo quinazolines were synthesized and reported for their binding affinity towards benzodiazepine and adenosine receptors. Some 1-methyl-4-(3-substitutedpropyl)-7,8-disubstituted-1,2,4-triazolo quinazolin-4(3H)-ones (225) were synthesized and studied for their enzyme inhibition activity. A series of novel non-classical reversed bridge quinazolines were synthesized and reported for their thymidylate synthetase inhibition activity.
The synthetic approach for 3-(substituted triazolo methyl)-2-alkyl-4-oxo quinazoline (226) derivatives\textsuperscript{335}, 2-substituted amino quinazolin-4-ones\textsuperscript{336}, 5,6,7,8-tetrahydro-2,6-diamino quinazolines\textsuperscript{337}, 2-vinyl-3H-quinazolin-4-ones\textsuperscript{338} and some 2-substituted aryl quinazolin-4(3H)-ones\textsuperscript{339} were described.

A novel isocyanate reaction on quinazolines\textsuperscript{340} (227) was led to the formation of unexpected cycloadducts. Series of substituted quinazolines\textsuperscript{341} were prepared and studied for their human adenosine A\textsubscript{3} receptor antagonistic activity.
The microwave enhanced synthetic technique was reported for 2-(2-amino phenyl)-4-amino quinazoline derivatives\textsuperscript{342} (228).

The synthesis of 2-substituted amino-3-(substituted phenyl) quinazolin-4(3H)-ones\textsuperscript{343} (229), some 5-chloro-2-methyl-3-(5-methylthiazol-2-yl)-4(3H)-quinazolone\textsuperscript{344} derivatives and 3-substituted amino-2-alkyl/aryl-4-oxo quinazolines\textsuperscript{345} (230) were reported.

In 2002, a new set of pyrazolo[1,5-c]quinazoline-2-carboxylates\textsuperscript{346} were synthesized and evaluated their excitatory amino acid antagonistic activity. In 2003, 4-amino-6-(hetero)arylalkylamino-1,2,4-triazolo[4,3-a]quinoxalin-1-one\textsuperscript{347} derivatives were synthesized and reported that these compounds exhibited a potent A(2A) adenosine receptor antagonists.

Some new 4-aryl-1,2,4-oxadizino[5,4-b]quinazolines\textsuperscript{348} (224) from 2-chloro quinazolin-4-one, some 1,2-disubstituted quinazolines\textsuperscript{349} (225) and some bismethaqualone, bismecloqualone and bispiroqualone analogues\textsuperscript{350} were synthesized and reported. Kant et al., prepared a series of 2,3-disubstituted quinazolines\textsuperscript{351} (226).
A series of [1,2,4] triazolo[1,5-c]quinazolines\textsuperscript{352} were screened for their adenosine antagonistic activity. In 2010, novel 6,7,8,9-tetrahydro-5H-5-phenyl-2-benzylidene-3-substituted hydrazino thiazolo(2,3-b)quinazoline derivatives were synthesized and screened for their anthelmintic activity. Novel quinazolinone derivatives also showed more potent antioxidant activity\textsuperscript{353, 354}. 