2. LITERATURE REVIEW

The name quinazoline (I) is universally used today to denote the 1,3-benzodiazine ring system. The name quinazoline (German chinazolin) was first proposed at the University of Leipzig in 1887 by Widdige on observing that his compounds were isomeric with the known cinnoline (II) and quinoxaline (III) derivatives.

Several structural modifications have been made to the quinazoline nucleus to enhance the biological activities like analgesic, anti-inflammatory, anticonvulsant, antibacterial, antifungal, antitubercular and antihistaminic activity, which attracted the attention of medicinal chemists. Herein a detailed survey of literature is described.
2.1 ANTIHISTAMINIC ACTIVITY

West and coworkers\textsuperscript{13} in 1981, synthesized 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 of having antihistaminic activity. These compounds showed significant antihistaminic activity.

In 1989, Lemura and coworkers\textsuperscript{14} synthesized the following 2-(4-substituted piperazinyl methyl)-3-substituted quinazolin-4-ones (2) and studied their antihistaminic activity.

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\end{center}

Fujio and coworkers\textsuperscript{15} in 1998, prepared some 2-amino-5,6,7,8-substituted quinazolines (3) with substituted amino group at 4\textsuperscript{th} position. These compounds were found to be exhibit antiallergic activity.

In the same year, Teruharu and coworkers\textsuperscript{16} synthesized a series of 2-amino-5,6,7,8-substituted quinazolines (4) by incorporating substituted amide group at 4\textsuperscript{th} position. The
pharmacological investigation of these compounds showed significant antiallergic activity.

In the year 1999, V. S. Kumar raju et al., synthesized the derivatives of 3-(N,N-dialkyl amino)-alkyl-2-phenyl quinazolin-4(3H)-ones (5) and evaluated for their H₁ antihistaminic activity. Among the synthesized compounds 3-(N,N-dibutylamino)-propyl-2-phenyl-quinazolin-4(3H)-one and 6-iodo-3-(N,N-dibutylamino)-propyl-2-phenyl-quinazolin-4-(3H)-one were found to be more potent.

In the year 2007, Gajbhiye et al., reported the 6-substituted chromon-[2',3',6,7]-[1,3,4]-thiadiazepin-[2,3-b]-6'-substituted quinazolin-4(3H)-ones (6). Entire synthesized
compounds exhibited significant inhibition of histamine induced contraction in guinea pig ileum in \textit{in vitro} studies. Among these compounds, 6'-bromo substitution contributed to the enhanced potency and 6-methyl substituent decreased the antihistaminic potency.

\[ (6) \]

In the year 2008, spiro-isobenzofuranones/2-substituted piperidino quinazolin-4-ones were discovered as potent, selective and brain penetrable non-imidazole H$_3$ receptor inverse agonist by M. Jitswoka$^{19}$ \textit{et. al.}, Their corporate sample collection was screened against the human H$_3$ receptor and results in identification of lead molecule. Incorporation of quinazolinone as left hand portion of lead molecule results in compound \textbf{(7)} which showed loss of activity.
In the year 2008, Mizutani et. al., developed some novel derivatives of 2-[4-(amino alkoxy)-phenyl]-quinazolin-4(3H)-ones (8) as potent and selective histamine H₃ receptor inverse agonists. Among these derivatives, compound (8) was found to be potent than standard compound.

In 2009, Alagarsamy and coworkers 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.
In 2010, M. Bhagawan raju\textsuperscript{22} \textit{et. al.}, prepared a series of 3-\([N,N\text{-dialkylamino}]{\text{alkyl}}\)-6-halo-2-thio-4(3\textit{H})-quinazolines \(\textbf{9}\), these compounds were found to possess H\(_1\)-antihistaminic activity.

\begin{equation}
\textbf{9}
\end{equation}

### 2.2 ANTIHYPERTENSIVE ACTIVITY

Kotto and coworkers\textsuperscript{23} in 1965, prepared a series of 2-substituted amino-5,6,7,8-substituted quinazolin-4-ones \(\textbf{10}\) with the aim of possessing antihypertensive activity. These compounds exhibited antihypertensive activity by inhibiting the angiotension converting enzyme.

Trimony and coworkers\textsuperscript{24} in 1968, synthesized a series of 2,6,7-trisubstituted quinazolin-4-ones and studied their antihypertensive activity. The compound 2-diethylamino-6,7-dimethoxy quinazolin-4-one \(\textbf{11}\) was found to be the most active agent in this series.
In 1985, Wamhoff and coworkers synthesized a series of 1,3,4-triazolo quinazolin-4-ones (12) and studied their antihypertensive activity. Among the series, compound 1,2,9-trimethyl-1,3,4-triazolo quinazolin-4(3H)-one was found to exhibit potent antihypertensive activity.
In 1986, Chien and coworkers\textsuperscript{26} synthesized some 1,3,4-triazolo quinazolin-4-ones (13) and evaluated antihypertensive property. The compound 2,9-dimethyl-1,3,4-triazolo quinzolin-4(3\textit{H})-one was found to be the most active antihypertensive agent in this series.

The same authors\textsuperscript{27} in 1988, synthesized a series of 1,2,4-triazolo quinazolines (14) and studied their antihypertensive activity. These compounds also showed antihypertensive activity ranging from 20.5 to 46.7\% with maximum activity when R was a thiol substituent.

Later, Ram and coworkers\textsuperscript{28} in 1990, prepared a series of 4-substituted-1,2,4-triazolo quinazolin-4-ones (15) with the piperazine moiety at 1\textsuperscript{st} position. These compounds were found to possess antihypertensive activity.

In 1993, Zhoghna\textsuperscript{29} reported the 1,7,8-trisubstituted-1,2,4-triazolo quinazolines (16) by placing substituted arylamine at 4\textsuperscript{th} position. Pharmacological investigation of these compounds showed significant antihypertensive activity.
In 1993, Chern and coworkers\textsuperscript{30} prepared some 2,3-dihydro imidazo[1,2-c] quinazolines for their antihypertensive property. These compounds were found to exhibit antihypertensive activity by blocking $\alpha_1$-adrenergic receptor.

In 1995, Pathak and coworkers\textsuperscript{31} prepared certain analogs of quinazolin-2,4-diones (17) with the substitution at 3\textsuperscript{rd} position. These compounds were reported to exhibit significant antihypertensive activity.

Harukazu and coworkers\textsuperscript{32} in 1996, synthesized a series of quinazolin-2,4-diones (18) by introducing arylsulfonyl moiety at 3\textsuperscript{rd} position and studied their antihypertensive activity. These compounds exhibited significant antihypertensive activity.
Jung Mou and coworkers\textsuperscript{33} in 1997, reported the synthesis of substituted imidazolo [1,2-c] quinazolines and studied their antihypertensive activity.

Rivero and coworkers\textsuperscript{34} in 1998, synthesized some 3-substituted quinazolin-2,4-diones (19) and investigated their antihypertensive activity. These compounds were found to exhibit significant activity.

The same authors\textsuperscript{35} in 1998, synthesized a series of fused quinazolines and 1,2,4-benzothiadiazine-1,1-dioxides with the aim of improving \(\alpha\)-adrenergic blocking activity. These compounds shown significant \(\alpha\)-adrenergic antagonistic activity.

In the year 1998, 2-methyl-3-[5-(substituted phenyl)triazoline]-4(3\(H\))-quinazolinones (20) as potential cardiovascular agents was reported by Ashok Kumar\textsuperscript{36} \textit{et. al.}, The most potent member of this series is 2-methyl-[3-imino-(2-fluoro phenyl)]-4(3\(H\))-quinazolinone.
In the year 1999, Alagarsamy et al., synthesized some novel 2-substituted[1,3,4]thiadiazolo[2,3-b]-6,7-disubstituted thieno [3,2-e]pyrimidin-5(4H)-ones (21) and evaluated their antihypertensive activity.

In 2000, Garcia and coworkers prepared a series of quinazolin-2,4-diones (22) with a substituted piperazine moiety at 3rd position. These compounds were found to exhibit antihypertensive activity.
In the year 2000, U. S. Pathak and Alagarsamy\textsuperscript{39} have reported the some 2-substituted [1,3,4]thiadiazolo[2,3-b]quinazolin-5(4\textsubscript{H})-ones (23) as antihypertensive agents.

![Chemical Structure](image)

(23)

In the year 2007, Alagarsamy\textsuperscript{40} et. al., reported the novel-3-benzyl-2-substituted-3\textsubscript{H}-[1,2,4]triazolo[5,1-b]quinazolin-9-ones (24) as antihypertensive agents. Among the test compounds 3-benzyl-2-methyl-[1,2,4]triazolo[5,1-b]quinazolin-9(3\textsubscript{H})-one exhibited significant antihypertensive activity.

![Chemical Structure](image)

(24)

In 2010, el-Sabbagh\textsuperscript{41} et. al., derived a series of octahydroquinazoline (25) and screened for their hypotensive activity, all the compounds, most of the compounds showed hypotensive activity.
2.3 ANTICANCER ACTIVITY

Robba and coworkers\textsuperscript{42} in 1974, prepared some \( N \)-[(4-amino-3,4-dihydro-4-oxoquinazoly)methyl]-\( N \)-prop-2-yl-amino]benzoyl-L-glutamic acid (26) and their derivatives as selective \textit{thymidylate synthetase} inhibitors. These compounds showed encouraging antitumor activity against breast and ovarian cancer in clinical trials.
Boyle and coworkers\textsuperscript{43} in 1993, reported the synthesis of some 2-methyl-6-substituted quinazolines. These compounds were found to exhibit antitumor activity.

Brana and coworkers\textsuperscript{44} in 1994, prepared a series of benzimidazo[1,2-c]quinazolines. When tested for anticancer activity, these compounds were found to exhibit potent antitumor activity.

Mang and coworkers\textsuperscript{45} in the same year synthesized some 2,4-diamino-6-substituted quinazolines (27) and studied their anticancer activity.

Arnold and coworkers\textsuperscript{46} in 1995, prepared a series of 4,5,6,7-tetra substituted quinazolines (28). These compounds were found to exhibit anticancer activity.

In 1997, Jones and coworkers\textsuperscript{47} synthesized a series of 3-chloro-\(N\)-[(3,4-dihydro-2-methyl-4-oxo-6-quinazolinyl)methyl]-4-phenyl sulphonyl]-\(N\)-(prop-2-nyl-)aniline and studied their antitumor activity.

In 1999, Kazuo and coworkers\textsuperscript{48} synthesized certain analogs of substituted quinazolines and studied their antitumor, antiatherosclerotic and antidiabetic activities.
Fathima and coworkers\textsuperscript{49} in 1999, reported the synthesis of 4-arylamino-6,7-disubstituted quinazolines (29) and studied their antitumor activity.

In the same year Papoulis and coworkers\textsuperscript{50} prepared a series of 2,4-diamino-6-(aryl methyl)-5,6,7,8-tetrahydro quinazolines (30). These compounds were reported to exhibit antitumor activity.

Raffa and coworkers\textsuperscript{51} in the same year reported the synthesis of some 3-(3-phenyl isoxazo-5-yl) quinazoline derivatives and studied their antineoplastic activity.
Hour MJ and coworkers\textsuperscript{52} in 2000, synthesized a series of 2,3-dihydro-3-methoxy-2-phenyl-4-quinazolinones \textbf{(31)} and studied their anticancer activity.

In the same year Lipunova and coworkers\textsuperscript{53} reported the synthesis of some novel fluorinated condensed quinazolines. These compounds were found to exhibit antitumor activity.

EL Sherbeny and coworkers\textsuperscript{54} in 2000, prepared a series of benzothiazol-[2,3-\textit{b}]-quinazoline derivatives \textbf{(32)}. These compounds were found to possess antitumor activity.

In the same year Wang YD and coworkers\textsuperscript{55} reported the synthesis, SAR and antitumor activity of a series of 4-subsitututed anilino-3-cyano-6,7-dimethoxy quinazolines \textbf{(33)}.

In 2001, Richard and coworkers\textsuperscript{56} synthesized and patented a series of 4-(3-ethyl phenylamino) quinazolines \textbf{(34)}. These compounds were found to possess anticancer activity.
In 2005, Ovadekova and coworkers\textsuperscript{57} evaluated 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.

In 2006, S. Jantova and coworkers\textsuperscript{58} reported that the effect of 3-(5-nitro-2-thienyl)-9-chloro-5-morpholin-4-yl[1,2,4]triazolo [4,3-c]quinazoline on cell growth, cell cycle, induction of DNA fragmentation and activity of caspase 3 in murine leukemia.

In 2006, Ghorab and coworkers\textsuperscript{59} synthesized some novel quinazoline derivatives bearing the biologically active thione moiety and these derivatives showed antitumor activity.

In 2008, Chinigo and coworkers\textsuperscript{60} synthesized 2,3-dihydro-2-arylquinazolin-4-ones (35) and found to possess potent fluorescent tubulin inhibition with anticancer activity.
In the same year Jantova and coworkers synthesized a series of 6-bromo-2-(morpholin-1-yl)-4-anilino quinazolines. These compounds showed antiproliferative activity.


Sirisoma and coworkers in 2009, synthesized \(N-(4-
\text{methoxy phenyl})-N-2\)-dimethyl quinazolin-4-amines (36), these compounds showed a great potency of anticancer activity.
Joseph Alex and coworkers\textsuperscript{64} in 2010, prepared a series of novel 3-(1,3,4-thiadiazol-2-yl)-quinazolin-4(3\textit{H})-ones and reported their anticancer activity.

In 2010, Jung and coworkers\textsuperscript{65} synthesized 3,4-dihydro quinazoline dihydrochloride (37) and these compounds exhibited antitumor activity.

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In 2010, Yan and coworkers\textsuperscript{66} prepared a highly functionalized 2,4-diamino quinazolines (38) and these derivatives showed anticancer and anti-HIV activity.

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In 2010, Giri and coworkers\textsuperscript{67} synthesized quinazolinone derivatives (39) and reported their anticancer activity.
In 2010, Tian and coworkers\textsuperscript{68} synthesized a series of 5,8-disubstituted quinazolines (40) and they were found to possess antitumor activity.

In 2010, Giri\textsuperscript{69} \textit{et. al.}, synthesized and evaluated some novel 2-thiophen-5-yl-3H-quinazolin-4-one (41) analogs as inhibitors of transcriptional activation.
Kamal et al., in 2010, prepared a series of quinazolines linked pyrrolo [2,1-c][1,4]benzodiazepine (42) conjugates and screened for their anticancer activity.

In 2010, Conconi and coworkers synthesized some fused tricyclic quinazolines and they showed antiangiogenic activity.

In 2010, Li and coworkers synthesized 2-chloromethyl-4(3H)-quinazolinone derivatives (43) and reported their anticancer activity.
In 2010, Boyapati and coworkers\textsuperscript{73} synthesized a novel 4-substituted quinazoline derivatives as DNA-gyrase inhibitors.

Kidwai and coworkers\textsuperscript{74} in 2010, synthesized a 2-oxo/thioxo octahydro quinazolin-5-one derivatives and they were reported that most of the compounds of this series shown significant anticancer activity.

In 2010, Vernones\textsuperscript{75} et. al., reported that 4-amino-tetrahydro quinazolino[3,2-e]purine derivatives (44) as anticancer agents.
In 2010, Sirisoma and coworkers\textsuperscript{76} synthesized $N$-methyl-4-(4-methoxy anilino)quinazolines (45) and reported that these compounds induced apoptosis.

In 2010, Ye Ding and coworkers\textsuperscript{77} synthesized some [4,8-disubstituted-8,9-dihydro pyrazine quinazoline-7(6$H$)-ketones and found to possess antitumor activity.

In 2010, Dou and coworkers\textsuperscript{78} synthesized a series of biquinazoline-2,2'-diones (46) and they exhibited \textit{in vitro} anticancer activity.
In 2010, Nandi et al. synthesized some of 4-anilino quinazoline derivatives and they showed anticancer activity.

In 2010, Abdel Gawad et al. synthesized some 2,3-disubstituted quinazolin-4(3H)-ones and 4,6-disubstituted-1,2,3,4-tetrahydro quinazolin-2H-ones (47, 48 and 49). These compounds were reported to possess antitumor activity.

In 2010, Garofalo and coworkers prepared a series of N-alkyl(anilino) quinazoline derivatives and evaluated for antitumor activity.
In 2010, El-Azab\textsuperscript{82} et al., synthesized some novel quinazoline derivatives (50) and screened for their antitumor activity.

\[ \begin{array}{c}
\text{Cl} \\
\text{N} \\
\text{N} \\
\text{X} \\
\text{R} \\
\end{array} \]

In 2010, Al-Omary\textsuperscript{83} et al., prepared a non-classical antifolates of 2,6-substituted-quinazolin-4(3H)-ones and these compounds were found to be exhibit good antitumor activity.

In 2010, YD Zhang\textsuperscript{84} et al., prepared a series of disubstituted dihydro pyrazino quinazoline derivatives and found to possess antitumor activity.

In 2011, AM. Alaseefya and coworkers\textsuperscript{85} reported that quinazoline derivatives having anticancer activity.

Perchellet and coworkers\textsuperscript{86} in 2011, synthesized some 2-halo-3-aryl-4(3H)-quinazolinium halides and these compounds showed antitumor activity.
In 2011, Thorat and coworkers\textsuperscript{87} synthesized 2,4-diaminoquinazoline derivatives (51), these derivatives showed protein 90 inhibitors.

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Chen and coworkers\textsuperscript{88} in 2011, synthesized 2,3-disubstituted-8-arylamino-3\textit{H}-imidazo quinazoline derivatives, they were reported to possess more potent antitumor activity.

In 2011, Li and coworkers\textsuperscript{89} synthesized 4-anilino quinazoline derivatives (52), these compounds possessed epidermal growth factor receptor tyrosine kinase activity.
In 2011, Chen et al., synthesized 6-fluoro-(3-fluoro phenyl)-4-(3-methoxy anilino) quinazoline and found to possess antimetastatic activity.

In 2011, Noolvi and coworkers prepared a series of substituted quinazolines derivatives and reported to possess in vitro antitumor activity.

In 2011, Kamal and coworkers synthesized 3,5-diaryl isoxazoline/isoxazole linked 2,3-dihydro quinazolin-4-ones and reported for their anticancer activity.
In 2011, X. Wu et al., prepared a series of novel 4-pyrrylamino quinazoline derivatives and screened for their antitumor activity.

In 2011, Beria and coworkers synthesized some 4,5-dihydro-1H-pyrazolo[4,3-H] quinazoline derivatives (55) and screened as potent and selective Polo-like kinase-1-inhibitor.

In 2011, Patel et al., prepared some substituted furoquinazoline derivatives (56) and these compounds were reported to possess in vitro antitumor activity.
In 2011, Marvania and coworkers\textsuperscript{96} synthesized some phenyl \(N\)-mustard quinazoline conjugates and evaluated for their antitumor activity.

### 2.4 ANALGESIC AND ANTI-INFLAMMATORY ACTIVITY

Lezlekovsky and coworkers\textsuperscript{97} in 1965, prepared a series of 4-phenyl-6,7,8,9-substituted-1,2,4-triazolo quinazolines (57) and studied their analgesic and anti-inflammatory activities.

In 1977, Yamamoto and coworkers\textsuperscript{98} synthesized some 1,5,7,8-tetrasubstituted-1,2,4-triazolo quinazolines (58). These compounds were reported to possess analgesic, anti-inflammatory, tranquilizing and antiviral activities.

In 1977, Koizomi and coworkers\textsuperscript{99} prepared a series of 2,6-disubstituted quinazolin-4-ones (59) as anti-inflammatory agents.
In 1978, G. Hardtman and coworkers\textsuperscript{100} synthesized and patented some 1,3,4-triazolo quinazolines (60). The pharmacological investigations of these compounds revealed their analgesic, anti-inflammatory, tranquillizing and antiviral activities.

Hardtman FG and coworkers\textsuperscript{101} in the same year prepared a series of 4,7,8-trisubstituted-1,3,4-triazolo quinazolines (61). These compounds exhibited anti-inflammatory, tranquillizing and antiviral activities.

Kottke and coworkers\textsuperscript{102} in 1988, prepared a series of 1,2,8,9-tetra substituted-1,3,4-triazolo quinazolines (62). These compounds were found to exhibit antirheumatic activity.

In 1988, the same authors\textsuperscript{103} also synthesized substituted triazolo quinazolinones (63). These compounds exhibited antirheumatic and antianaphylactic activities.
Kamal and coworkers\textsuperscript{104} in 1988, reported the synthesis of some 1,5,7-trisubstituted-1,2,4-triazolo quinazolines (64). These compounds shown both analgesic and anti-inflammatory activities.

Nigam and coworkers\textsuperscript{105} in 1991, synthesized some 3-substituted aryl-2,6-disubstituted quinazolines (65). These compounds exhibited anti-inflammatory activity.
In 1993, Srivastava and coworkers\textsuperscript{106} prepared a series of substituted indolyl quinazolin-4-ones and studied their analgesic and anti-inflammatory activities.

In the year 1994, a large number of new ethyl-1-methyl-5-[4-oxo-3(4\textit{H})-quinazoliny]-1\textit{H}-pyrazole-4-acetates were prepared and its analgesic activity was evaluated by G. Daidone\textsuperscript{107} \textit{et. al.}, Among the synthesized compounds (66), 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.
Hitkari and coworkers\textsuperscript{108} in 1995, synthesized some 6-substituted-2-alkyl-3-(4-amino benzene sulphonamido) quinazolin-4-ones (67). These compounds showed anti-inflammatory activity.

In 1996, Peter and coworkers\textsuperscript{109} reported a series substituted quinazolines (68) by incorporating amino group at 4\textsuperscript{th} position. These compounds were found to possess anti-inflammatory activity.

Hiroshi and coworkers\textsuperscript{110} in 1996, prepared certain analogs of substituted dioxoquinazolines. These compounds were reported to possess anti-inflammatory activity.

Saravanan and coworkers\textsuperscript{111} in 1998, prepared some 2,3-disubstituted-6-bromo quinazolin-4-ones (69) and studied their anti-inflammatory activity.

Rity and coworkers\textsuperscript{112} in 1998 prepared certain analogs of 2-methyl-3-substituted quinazolin-4-ones (70) and studied their anti-inflammatory activity.
Bothra and coworkers\textsuperscript{113} in 1998, prepared some substituted quinazolines and tested them for their anti-inflammatory activity.

Bekhit and coworkers\textsuperscript{114} in the same year synthesized some novel benzopyrazolyl, benzoaxazolyl, quinazolinyl derivatives of quinazolin-4-ones. These compounds exhibited anti-inflammatory activity.

Junichi and coworkers\textsuperscript{115} in 1998, synthesized a series of substituted quinazolines. These compounds were found to exhibit analgesic activity.

In the year 1998, some new isatin hydrazones (71) containing different heteroaryl group such as 2-substituted
quinazolinyl acetic acid hydrazide and benzoazinonyl acetic acid hydrazide were prepared by M. Sarangapani et al., Analgesic activity of the test compounds were assayed by acetic acid induced writhing method. Among these synthesized compounds, compound 7-methyl isatin-3-[N-2-(2-phenyl-3,4-dihydro-4-oxo-quinazolin)-3-methyl carbonyl]-hydrazone was the potent compound of this series.

![Chemical Structure](image)

In 1999, Qi Deng coworkers reported the synthesis of some 3-substituted quinazolin-4-ones. These compounds showed anti-inflammatory activity.

Ramasharma and coworkers in 1999, prepared a series of 3-(thiadiazolylamino)-2,6,8-trisubstituted quinazolin-4-ones and studied their anti-inflammatory activity.

Giedrute and coworkers in 1999, synthesized some 4-(substituted anilino) quinazolin-2-carboxylates and studied their anti-inflammatory activity.

Abdelal and coworkers in 2001, prepared a series of 1,2,4-triazolo[4,3-c]quinazolines. When evaluated for their
CNS activities these compounds showed both analgesic and anticonvulsant activities.

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\text{(72)}
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\text{(73)}
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\text{(74)}
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In the same year to improve the properties of 6,7,8-unsubstituted quinazolinone (66), G. Daidone et al., prepared a new series of compounds (75) which are substituted on the quinazolinone nucleus with groups that have similar lipophilic character but exert opposite electronic effects. The pharmacological data obtained for these compounds (75) were compared with previously reported unsubstituted analogs compound (66). 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(4\textsubscript{H})-yl)-1-methyl-1\textsubscript{H}-pyrazol-4-yl)-acetate.
In the year 2002, Alagarsamy et al., synthesized some novel 1-[2-phenyl quinazolin-3-yl-4(3H)-one]-3-(substituted)-thiourea (76) and evaluated its analgesic and anti-inflammatory activity. Biological evaluation of these compounds showed significant analgesic and anti-inflammatory activities.

In the year 2003, Alagarsamy et al., prepared a series of substituted quinazolin-4(3H)-ones by replacing the phenyl group with methyl group at 2nd position (77). Biological evaluation of these compounds exhibited more significant analgesic and anti-inflammatory activities than the phenyl substituted series.
In the year 2003, Alagarsamy et al., prepared a series of 2-benzylamino-3-(substituted)-quinazolin-4-(3H)-ones (78) by incorporating the benzylamino group instead of phenyl group at 2nd position of quinazolinones. The compound 2-(benzylamino)-3-(3-phenyl allylideneamino)-quinazolin-4(3H)-one is found to be the most active analgesic agent and it is equipotent with standard diclofenac sodium.

Ashok kumar et al., in the year 2003, reported the synthesis of novel quinazolinone derivatives (79) and evaluated for their analgesic activity. The report shown that 2-(ω-chloro acetonyl)-3-substitutedphenyl-6-halo/6,8-dihaloquinazolin-4-(3H)-ones exhibited mild to moderate activity at a dose of 50 mg/kg p.o. Whereas, the hydrazino products of i.e. 2-(ω-hydrazino acetonyl)-3-substitutedphenyl-6-halo/6,8-dihalo...
quinazolin-4-(3\textit{H})-ones (80) exhibited poor activity. However the pyrazoline derivatives of parent compound (81) exhibited more potent activity than (79) and (80).

Some new 2,3,6-trisubstituted quinazolinones were synthesized by Ashok kumar$^{126}$ \textit{et. al.}, in the same year, 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 (82) exhibited mild to moderate analgesic activity. Furthermore, cyclisation of (82) into their corresponding compound (83) results in increased activity.

In the year 2003, Panneer selvam\textsuperscript{127} et. al., reported the synthesis of novel 2-methyl quinazolin-4-(3\textit{H})-ones (84) and evaluated for their analgesic activity. The activity was determined by tail-immersion method in mice at three doses level (100, 200 and 400 mg/kg p.o.). The results were compared with standard pentazocine at a dose of 10 mg/kg i.p. dose. The
results of biological activity showed that the entire synthesized compounds (84) exhibited only mild analgesic activity.

In the year 2004, Alagarsamy et. al., prepared a series of 1-[2-methyl thio quinazolin-3-yl-4(3H)-one]-3-(substituted) thiourea (85). The results clearly revealed that the 2-methylthio quinazolinones exhibited better activity than the earlier reported compounds. The potent compound of this series was 1-[2-methylthio quinazolin-3-yl-4(3H)-one]-3-diethyl thiourea, which exhibited more activity than standard diclofenac sodium.

Later in the same year by using isosteric principle Alagarsamy et. al., prepared some novel 2-mercapto-3-(substitutedamino)-5,6,7,8-tetrahydro-3H-benzo[4,5]-thieno-
(2,3-d)-pyrimidin-4-ones (86) and evaluated its analgesic activity [thienopyrimidine is bioisostere of quinazoline].

![Chemical Structure](image)

In the year 2006, studies on some biologically active 6,8-disubstituted-2-phenyl-3-[substituted-benzothiazol-2-yl]-4(3H)-quinazolinones (87 and 88) were reported by S. S. Laddha et al. All newly synthesized compounds were tested for their anti-inflammatory activity. However, they were found all compounds are less potent when compared to standard drug.
In the year 2007, E. M. Jessy et al., reported the synthesis of some novel quinazolinones (89) and tested for their anti-inflammatory activity. All the compounds exhibited good activity ranging from 62.2 to 80.7% reduction in edema volume compared to standard ibuprofen at 200 mg/kg dose.

In the year 2007, effect of incorporating thiazolidinone and azetidinone on anti-inflammatory activity of novel quinazolin-4-(3H)-ones was studied by Ashok kumar et al., using carrageenan induced paw edema method in rats. All the compounds (90 and 91) exhibited anti-inflammatory activity of varying degree from 16.3 to 36.3%.
Later in the year 2007, analgesic activity of 3-[4′-(p-chlorophenyl)-thiazol-2'-yl]-2-[(substituted azetidinone/thiazolidinone)-aminomethyl]-6-bromo quinazolin-4-ones was studied by Ashok Kumar et al., using acetic acid induced writhing test on mice at a dose of 50 mg/kg p.o. to evaluate analgesic activity of synthesized compounds. All the synthesized compounds (92) exhibited mild analgesic activity.
In 2007, P. S. Reddy et al., synthesized some substituted quinazolinones (93) and evaluated their analgesic activity by acetic acid induced writhing method. The analgesic data of this study indicated that introduction of 2'-aminophenyl at N-1 of quinazolinone does not increase the activity because the entire derivatives exhibited only mild to moderate activity.

In 2007, Alagarsamy et al., synthesized some 3-(4-methyl phenyl)-2-substituted amino quinazolin-4(3H)-ones (94) and studied their analgesic and anti-inflammatory activities.
In 2008, Altenbach and coworkers\textsuperscript{136} were synthesized cis-4-(piperazin-1-yl)-5,6,7a,8,9,10,11,11a-octahydro benzofuro[2,3-\textit{H}] quinazolin-2-amines. These compounds showed more potent histamine H\textsubscript{4} antagonistic activity that blocks pain responses against carrageenan-induced hyperalgesia.

Alagarsamy and coworkers\textsuperscript{137} in 2008, synthesized a series of 3-(4-ethyl phenyl)-2-substituted amino quinazolin-4(3\textit{H})-ones \textbf{(95)} as a novel class of analgesic and anti-inflammatory agents.
In 2008, Fathalla and coworkers\textsuperscript{138} synthesized a series of quinazolin-4(3\textit{H})-one derivatives and studied their antimicrobial and anti-inflammatory activities.

Alafeefy and coworkers\textsuperscript{139} in 2008, prepared a series of new 3\textit{H}-quinazolin-4-one derivatives and studied their analgesic and anti-inflammatory activities.

Alagarsamy\textsuperscript{140} \textit{et. al.}, in 2008, synthesized some 3-(2-pyridyl)-2-substituted-quinazolin-4(3\textit{H})-ones (96) and evaluated for their analgesic and anti-inflammatory activities.

\begin{center}
\includegraphics[scale=0.5]{fig96.png}
\end{center}

In 2009 MS. Mohamed\textsuperscript{141} \textit{et. al.}, prepared a series a novel 3-(p-substituted phenyl)-6-bromo-4(3\textit{H})-quinazolinones. These compounds showed promising anti-inflammatory and analgesic properties.

Alagarsamy\textsuperscript{142} \textit{et. al.}, in 2009, prepared some 3-cyclohexyl-2-substituted hydrazino quinazolin-4(3\textit{H})-ones (97) and studied their analgesic and anti-inflammatory activities.
In 2009, Alagarsamy and coworkers\textsuperscript{143} prepared a series of 3-(3-ethyl phenyl)-2-substituted hydrazino-3\textit{H}-quinazolin-4-one derivatives (98). These compounds were exhibited potent analgesic and anti-inflammatory activities.

Giri and coworkers\textsuperscript{144} in 2009, prepared some novel 2-(2,4-disubstituted-thiazole-5-yl)-3-aryl-3\textit{H}-quinazoline-4-one derivatives (99) and screened for their anti-inflammatory activity.
El-Gazzar and his coworkers in 2009, synthesized some azolopyrimidoquinolines, pyrimido quinazolines and reported that these compounds showed anti-oxidant, anti-inflammatory and analgesic activities.

Giri et. al., in 2009, prepared a series of novel 2-thiophen-5-yl-3H-quinazolin-4-one analogs and reported that these compounds possess anti-inflammatory and anti-cancer activities.

In 2010, MM. Ghorab et. al., synthesized some novel triazolo quinazolines and triazino quinazolines containing
benzene sulfonamide moieties and reported these compounds showed good antipyretic and anti-inflammatory activities.

Boyapati and coworkers\textsuperscript{148} in 2010, prepared some novel 4-substituted quinazolines and performed for antimicrobial and DNA-gyrase inhibitor activities.

Alafeefy\textsuperscript{149} \textit{et al.}, in 2010, synthesized novel quinazoline derivatives (102) and evaluated for their analgesic and anti-inflammatory activities.

In 2010, Panneer selvam\textsuperscript{150} \textit{et al.}, synthesized a novel 6,7,8,9-tetrahydro-5\textit{H}-5-hydroxy phenyl-2-benzylidin-3-substituted hydrazino thiazolo(2,3-b)quinazolines and studied their antioceptive and anti-inflammatory activities.
Hunoor and coworkers\textsuperscript{151} in 2010, prepared a series of 2,3-disubstituted 1,2-dihydro quinazolin-4(3\textit{H})-one derivatives and screened for their anti-inflammatory and analgesic activities.

In 2010, Stephen rathinaraj\textsuperscript{152} \textit{et. al.}, prepared a series of 6-bromo-2-phenyl-3-substituted-4-quinazolinone derivatives (103) and studied their anti-inflammatory, analgesic and antibacterial activities.

\[
\text{Br} \quad \text{CONHR} \\
\begin{array}{c}
\text{N} \\
\text{O} \\
\text{CH}_2\text{CONHR}
\end{array}
\]

\textit{(103)}

Sabbagh and coworkers\textsuperscript{153} in 2010, prepared some 2,3-dihydro quinazolin-4(1\textit{H})-one derivatives and screened for their analgesic and anti-inflammatory activities.

In 2010, Hoonur and coworkers\textsuperscript{154} prepared a series of some 3-aryl-2-substituted-1,2-dihydro quinazolin-4(3\textit{H})-one derivatives. These compounds showed a potent analgesic and anti-inflammatory activities.

In 2010, Amini and coworkers\textsuperscript{155} prepared a series of spiro\{[2\textit{H}, 3\textit{H}] quinazoline-2,1'-cyclohexan\}-4(1\textit{H})-one
derivatives and applied for docking studies. These compounds exhibited anti-inflammatory and analgesic activities.

BA. Rather and coworkers\textsuperscript{156} in 2010, prepared some novel 2-substituted-quinazolin-4(3\textit{H})-ones and evaluated for their analgesic and anti-inflammatory activities.

Hunoor\textsuperscript{157} \textit{et al.}, in 2010, synthesized some of new 2,3-disubstituted-1,2-dihydro quinazolin-4(3\textit{H})-one derivatives and studied their anti-inflammatory and analgesic activities.

Mosaad and coworkers\textsuperscript{158} in 2010 prepared some novel 6,8-dibromo-4(3\textit{H})-quinazolinone derivatives. These derivatives exhibited potent anti-inflammatory and analgesic properties.

Mohamed and coworkers\textsuperscript{159} in 2011, prepared a series of quinazolin-4(1\textit{H})-one derivatives and studied their anti-inflammatory and analgesic activity.

In 2011, Kumar\textsuperscript{160} \textit{et. al.}, synthesized a new three-component reaction of novel isoindolo[2,1-a]quinazolines and these compounds showed a potent inhibitors of TNF-\textalpha.

\textbf{2.5 ANTVIRAL ACTIVITY}

In the year 2002, GA. El-Hiti\textsuperscript{161} \textit{et. al.}, reported the synthesis and reactions of some 3-aryl-2-thioxo-quinazolin-4(3\textit{H})-ones (104). The results clearly indicated that out of six
test compounds, three compounds are active against three cell-
lines when tested at one dose primary anticancer assay
including lung, breast and CNS.

In the year 2004, anti-HIV activities of some novel 2,3-
disubstituted quinazolin-4(3H)-ones (105) were reported by
Alagarsamy\textsuperscript{162} \textit{et. al.}, Compound 2-mercapto-3-\{[benzimidazol-1-
yl]-methylamino\} -quinazolin-4-(3\textit{H})-one and 2-mercapto-3-
{[(aniline-\textit{N}-yl)-methylamino]}-quinazolin-4-(3\textit{H})-one exhibited
maximum 31\% and 25\% protection respectively against HIV-1.
Whereas, 2-mercapto-3-\{[pyridine-2-yl]-methylamino\}
-quinazolin-4-(3\textit{H})-one showed 27\% protection against HIV-2.

In the year 2004, thiadiazolyl quinazolones (106) were
synthesized by V. K. Pandey\textsuperscript{163} \textit{et. al.}, as potential antiviral
agents. These compounds were evaluated against Japanese Encephalitis Virus (JEV) and Herpes Simplex Virus-1 (HSV-1) via in vitro method using mice. Compounds containing R= n-propyl was found to more active against JEV.

In the year 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 (107) were reported by P. Selvam\textsuperscript{164} et. al., Results revealed that none of the test compounds exhibited anti-HIV activity; whereas, entire test compounds displayed cytotoxic properties in MT-4 cells i.e. EC\textsubscript{50} values of test compounds against the replication of HIV-1 and HIV-2 in acutely infected MT-4 cells were higher than CC\textsubscript{50}.
In the year 2005, D. Kim et al., discovered a series of 1,3,4-trisubstituted pyrrolidines. They studied the effect of fused heterocycles on antiviral activity and pharmacokinetic properties. Imidazopyridine derivative caused eight fold more potent than its regioisomer. Incorporation of carbonyl group into benzimidazole derivative results in the formation of quinazolinone compounds (108). But this compound exhibited very less activity than benzimidazole derivative.

![Chemical Structure](image)

(108)

In the year 2005, isoquinolinyl quinazolines (109) were synthesized and its antiviral activity was evaluated by V. K. Pandey et al., These compounds were tested against Influenza virus in embryonated hen’s egg at the concentration of 0.5 mg embryo in allantoic cavity. From the results it was found that these compounds showed varying degree of antiviral activity.
In the year 2005, synthesis of non-classical quinazolinones \( (110) \) as thymidylate synthase inhibitors and their \textit{in vitro} antitumor activity was evaluated by D. J. Baek\textsuperscript{167} \textit{et. al.}, The biological activities of the compounds \( (110) \) were evaluated for the inhibition against bacterial \((L. casei)\) TS and/or human TS and for the cell growth inhibition of tumor cell lines of murine and human origin \textit{in vitro}. 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 \( \mu \text{M} \) and 0.003-0.03 \( \mu \text{M} \) respectively.
In the year 2005, R. Girija et al., synthesized 3-[5-amino-6-(2,3-dichloro phenyl)-[1,2,4]-triazin-3-yl]-6,8-dibromo-2-substituted quinazolin-4(3H)-ones (111) and evaluated its anticancer activity. 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<sub>50</sub>: 2.65 µg/ml) among the compounds tested.

In the year 2005, synthesis and \textit{in vitro} antitumor activity of novel quinazolin-4(3H)-one derivatives with dithiocarbamate side chain (112) was studied by S. L. Cao et al., The synthesized derivatives were 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<sub>50</sub> values ranging from 0.5 to 31 µM.
In the year 2006, A series of 5-(3',4',5'-substituted)-anilino-4-hydroxy-8-nitro quinazolines (113) were designed and synthesized to investigate the effect of the substitution on the inhibitory activity against mitotic progression of tumor cells were reported by Y. Jin et al. The effect of compounds (113) on the proliferation of cell was evaluated using MTT assay. 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 µM.

In the year 2006, M. J. A. De Jonge et al., reported the phase-I and pharmacokinetic studies of halofuginone (114) in
patients with advanced solid tumors and the compound has entered into phase-II study.

\begin{center}
\includegraphics[width=0.5\textwidth]{image1.png}
\end{center}

(114)

In the year 2006, synthesis, DHF reductase inhibition, antitumor testing and molecular modeling studies of some new quinazolin-4-(3\(H\))-ones (115) were reported by S. T. Al-Rashood\textsuperscript{172} et. al., All the compounds exhibited activity with IC\textsubscript{50} values ranging from 0.4 to 70 \(\mu\)M. Compound (116) exhibited more activity than other compounds.

\begin{center}
\includegraphics[width=0.5\textwidth]{image2.png}
\end{center}

(115)

(116)
In the year 2006, 1,3,5-tri-p-[(2-aryl-3H-quinazolin-4-one-3-yl)-phenyl]-2,4,6-hexahydro-1,3,5-s-triazines \((117)\) were synthesized as potential anti-TMV agents by VK. Pandey\textsuperscript{173} \textit{et. al.}, Four title compounds were screened for their antiviral activity against Tobacco Mosaic Virus (TMV) from the host \textit{Nicotiana tabacum} CV Samsun 'NN'. All the title compounds were found to be active against TMV.

\[
\begin{align*}
\text{\textsuperscript{R}} \quad \text{\textsuperscript{R}} \\
\text{\textsuperscript{O}} \quad \text{\textsuperscript{O}} \\
\text{\textsuperscript{N}} \quad \text{\textsuperscript{N}} \\
\text{\textsuperscript{N}} \quad \text{\textsuperscript{N}} \\
\text{\textsuperscript{N}} \quad \text{\textsuperscript{N}} \\
\text{\textsuperscript{N}} \quad \text{\textsuperscript{N}} \\
\text{\textsuperscript{N}} \quad \text{\textsuperscript{N}} \\
\end{align*}
\]

(117)

In the same year VK. Pandey\textsuperscript{174} \textit{et. al.}, synthesized quinazolinyl syndones \((118)\) and evaluated for their antiviral activity. The test compounds were evaluated against JEV and HSV-1 \textit{in vitro} method. Phenyl and styryl substituent was found to be the same effect for anti-HSV-1 activity.
In the year 2006, biological activity of oxo/thiono triazolo isoquinolinyl quinazolones (119) were studied by A. Bishnoi et al., Compounds (119) were screened for their antiviral activity against Influenza virus. The results showed that test compounds exhibited varying order of antiviral activity.

In the year 2006, synthesis of some amino acids incorporated quinazolin-4-((3\text{H})-one (120) as possible antiherpes viral agents were reported by S. N. Meyyanathan et al., This compound was tested for in vitro antiviral activity against Herpes Simplex Virus type-1 (HSV-1) using CPE inhibition assay. Among the test compounds, proline derivative exhibited good protection till 72 h at the concentration of 300 and 400 \mu g/ml.
In the year 2007, synthesis and antiviral activity of 2-aryl/methyl-3-(substituted benzylamino)-quinazolin-4-(3H)-ones (121) were reported by X. Gao\textsuperscript{177} \textit{et. al.}, Compounds having $R_1 = 4$-CF\textsubscript{3} showed curative rates of 55 and 54\% which was slightly higher than that of reference (54\%) against TMV at 500 \(\mu\text{g/ml}\) concentration.

In the year 2007, thiophene analogs of 5-chloro-5,8-dideazafolic acid (122) and 2-methyl-2-desamino-5-chloro-5,8-dideazafolic acid (123) were synthesized by R. A. Forsch\textsuperscript{178} \textit{et. al.}, and they evaluated for their \textit{in vitro} antitumor activity.
In 2007, Gao et al., synthesized a series of 2-aryl- or 2-methyl-3-(substituted benzylamino)-4(3H)-quinazolinone derivatives and performed for their antiviral activity.

Lyakhova and coworkers in 2009, prepared a series of phenyl benzimidazoles and benzoimidazo[1,2-c]quinazolines and reported their antiviral activity.

In 2010, Kumar and coworkers synthesized and reported the antiviral activity and cytotoxicity evaluation of schiff bases of some 2-phenyl quinazoline-4(3H)-ones.

Zhu et al., in 2010, synthesized a novel series of 2,4-diaryl-4,6,7,8-tetrahydro quinazolin-5(1H)-one derivatives and reported that these compounds showed as anti-HBV agents.
In 2011, Sakthi saravananan et al. synthesized a series of 2-phenyl-3-substituted quinazoline-4-(3H)-ones and these compounds were showed more potent antiviral and cytotoxicity effects.

In 2011, Krishnan and coworkers prepared a series of 2-phenyl-3-substituted quinazolin-4(3H)-ones and these compounds screened for their antiviral and cytotoxic activities.

2.6 CNS ACTIVITY

Jackman and coworkers in 1960, prepared some 2-methyl-3-(o-tolyl) quinazolin-4(3H)-ones and 2-methyl-3-(o-chlorophenyl) quinazolin-4(3H)-ones (124). These compounds were reported to possess sedative, hypnotic and anticonvulsant activities.

![Chemical structures](image)

Chaurasia and coworkers in 1982, prepared a series of 3-(2-benzthiazolyl)-2,6-disubstituted quinazolin-4(3H)-ones
These compounds were found to exhibit CNS depressant activity.

Tanabe Seiyaku\textsuperscript{187} in 1985, synthesized some 2-fluoromethyl-3-substituted phenyl-6-amino quinazolin-4(3\textit{H})-ones (126), when evaluated for their CNS activities these compounds were found to possess CNS depressant activity.

Certain analogs of 2-substituted thio-3-substituted phenyl quinazolin-4-(3\textit{H})-ones (127) with chloro group at C–7 position were prepared by Lakhan and coworkers\textsuperscript{188} in 1989. These compounds were reported to possess CNS depressant activity.

\[
\begin{align*}
\text{(126)} & \quad \text{(127)} \\
\ \quad & \quad \\
\end{align*}
\]

In 1996, Abdul Hamid and coworkers\textsuperscript{189} prepared a series of 2-(((5-ethyl-5-phenyl-1-barbituryl) methyl) carbonyl) thio-3,6,8-trisubsituted quinazolin-4(3\textit{H})-ones (128). These compounds were reported to possess anticonvulsant activity.
Ibrahim\textsuperscript{190} in 1998, synthesized a series of 3-substituted-6,8-dichloro-2-phenyl-4(3\textit{H})-quinazolines (129) and studied their anticonvulsant activity. These compounds were found to possess good anticonvulsant activity.

Hassanein and coworkers\textsuperscript{191} in 1998, synthesized some 1,3-disubstituted quinazolin-2,4-diones (130). When evaluated for their anticonvulsant activity, these compounds were found to possess anticonvulsant property.

In the same year, Nawrocka and coworkers\textsuperscript{192} prepared a series of substituted quinazoline-4-ones. The pharmacological investigation of these compounds showed anticonvulsant activity as expected.
Cyrilo and coworkers\textsuperscript{193} in 2000, synthesized some acetylenic quinazoline derivatives and screened for their anticonvulsant activity. These compounds were found to possess anticonvulsant activity as expected.

In 2001, Kumar and coworkers\textsuperscript{194} synthesized some 3-(substituted phenyl)-2-substitutedmethyl-4-oxo quinazolines (131) and studied their antiparkinsonism activity.

In the year 2003, M. Zappala\textsuperscript{195} et. al., synthesized a series of 7,8-methylenedioxy-4H-2,3-benzodiazepin-4-ones (a) and 6,7-methylenedioxy phthalazin-1-(2H)-ones (132). These compounds were found to possess excellent anticonvulsant activity.

\[
\begin{align*}
\text{(132)}
\end{align*}
\]

In the year 2004, in order to develop more potent anticonvulsant agents with minimum or no side effects, Archana\textsuperscript{196} et. al., planned to synthesize a series of compounds having two heterocyclic moieties such as quinazolinone and 2-oxo/thiobarbituric acid into a single molecular framework. The results of anticonvulsant activity of 3-(amino ethyl ethanoate)-2-methyl-6-mono/6,8-dihalo substituted quinazolin-4-(3H)-ones
(133) exhibited less activity at a dose of 50 mg/kg i.p. in MES and PTZ induced seizures. Whereas thiosemicarbazide of (133) 1-[3-substituted-2'-methyl-6'-mono/6',8'-dihalo substituted quinazolin-4'-(3'H)-ones (134) exhibited more anticonvulsant activity in both models (134).

![Chemical structures of (133) and (134)](image)

In the year 2005, synthesis and isolation of new regioisomeric 4-thiazolidinones (135) and (136) and their anticonvulsant activity was reported by A. Gursoy et. al., Among these synthesized compounds, selected members of thiazolidinone were screened and found to possess moderate anticonvulsant activity.

![Chemical structure of (135)](image)
In the year 2006, synthesis and pharmacological screening of some substituted benzothiazole derivatives of thioquinazolinone (137) was reported by H. H. Patel et al., The anticonvulsant activity of test compounds clearly indicated that iodo derivatives shown more activity than bromo derivatives.

In the year 2008, V. Jatav et al., reported the synthesis and anticonvulsant activity of some novel 3-[5-substituted-1,3,4-thiadiazol-2-yl]-2-styryl quinazolin-4(3H)-ones (138). Out of eighteen synthesized compounds, only six compounds were found to exhibit anticonvulsant activity in MES method.
In the same year authors continued their above studies and Jatav\textsuperscript{200} \textit{et. al.}, reported the anticonvulsant activity of some novel quinazolinone \textbf{(139)}. But, the new compounds \textbf{(139)} also produced less anticonvulsant activity whereas, the same new compounds exhibited better sedative-hypnotic activity and CNS depressant activities.

\begin{center}
\includegraphics[width=0.8\textwidth]{138.png}
\end{center}

In 2009, Kashaw and coworkers\textsuperscript{201} were synthesized some new bioactive 1-(4-substituted-phenyl)-3-(4-oxo-2-phenyl/ethyl-4\textit{H}-quinazolin-3-yl) ureas. These compounds were found to possess anticonvulsant and CNS depressant activities.

\begin{center}
\includegraphics[width=0.8\textwidth]{139.png}
\end{center}

In 2010 S. N. Pandya\textsuperscript{202} \textit{et. al.}, prepared some novel 3-[(substituted)-amino]-2-2-phenyl-3\textit{H}-quinazolin-4-ones and studied their anticonvulsant and neurotoxicity effects.
In 2010, Markosyan\textsuperscript{203} \textit{et. al.}, in 2010 synthesized some new spiro-derivatives of benzo[$H$] quinazolines and these derivatives found to possess antineoplastic and anti monoamino oxidase activities.

Panneer selvam\textsuperscript{204} \textit{et. al.}, in 2011, synthesized some novel 6,7,8,9-tetrahydro-5$H$-5-(2'-hydroxy phenyl)-2-(4'-substituted benzylidene)-3-(4-nitro phenylamino) thiazolo quinazoline derivatives and studied their anticonvulsant activity.

Shrivastava\textsuperscript{205} \textit{et. al.}, in 2011, synthesized a novel 2-(substituted)-3-[(substituted)amino] quinazoline-4(3$H$)-ones (140) and studied their psychomotor seizure activity.

![Chemical structure of 140](image)

2.7 MISCELLANEOUS ACTIVITIES

Franchis and coworkers\textsuperscript{206} in 1988, synthesized some substituted-1,3,4-triazolo quinazolines (141), when evaluated
for their adenosine antagonistic activity, these compounds were found to possess significant adenosine antagonistic activity.

![Chemical Structure](141)

In 1991, Francis JE and coworkers\textsuperscript{207} synthesized a series of novel [1,2,4]triazolo[1,5-c]quinazolin-5(6\textit{H})-ones and reported their binding affinity towards benzodiazepine receptor.

Takasa and coworkers\textsuperscript{208} in 1993, prepared a series of 4-(substituted benzylamino)-6,7,8-trimethoxy quinazolines (142). Biological investigation of these compounds showed good cGMP-PDE inhibition activity.

In the year 1993, Gatta\textsuperscript{209} prepared some substituted-1,2,4- triazolo quinazolines (143). These compounds were reported to possess affinity towards adenosine and benzodiazepine receptors.
In 1995, Splegel and coworkers\textsuperscript{210} prepared some 2-substituted-4-(substituted anilino) quinazolines (144) and studied their affinity towards nerve growth factor.

Lee and coworkers\textsuperscript{211} in the same year prepared a series of 2-(pyridyl/imidazolyl)-4-(substituted anilino) quinazolines (145). These compounds were reported to possess cGMP-PDE inhibition activity.

Kaddachi and coworkers\textsuperscript{212} in 1995, described the synthesis of some 3,5,6,7,8-substituted quinazolin-2,4-diones (146).
In 1995, synthesis of certain analogs of 3-(2-mercaptoethyl) quinazolin-2,4-diones (147) were reported by Gutschow and coworkers.\textsuperscript{213}

Gazit and coworkers\textsuperscript{214} in 1996, synthesized some 4-substituted anilino quinazolines (148) and studied their enzyme inhibition activity. These compounds were reported to possess significant tyrosine kinase inhibition activity.

In 1996, Kim YC and coworkers\textsuperscript{215} reported the selectivity of derivatives of the triazoloquinazoline adenosine antagonist towards human A3 receptor subtype.

In 1996, G. Biagi and coworkers\textsuperscript{216} synthesized 1,2,3-triazolo[1,5-a]quinazolines and reported their binding affinity towards benzodiazepine receptor.

Denny and coworkers\textsuperscript{217} in the same year prepared a series of 4-substituted anilino quinazolines (149) and also substituted at 3\textsuperscript{rd} position. These compounds were found to possess good tyrosine kinase inhibition activity.
In the same year, Rewcastle and coworkers\textsuperscript{218} synthesized some 4-substituted anilino quinazolines (150) with methoxy group at 7\textsuperscript{th} and 8\textsuperscript{th} positions. These compounds were reported to exhibit tyrosine kinase inhibition activity.

In 1996, Gabor and coworkers\textsuperscript{219} reported the synthesis of 5,6,7,8-tetrahydro quinazolin-4(3H)-one derivatives.

Gray and coworkers\textsuperscript{220} in 1996 described the synthesis of certain analogs of substituted quinazolines.

Hashash and coworkers\textsuperscript{221} in 1996, reported the synthesis of 2-substituted quinazolin-4(3H)-thione derivatives and studied their biological activity.
Bertrand and coworkers\textsuperscript{222} in 1997, synthesized some 3-(2-chlorophenyl)-2-(substitutedpyridinyl)-6-fluoroquinazolin-4(3\textit{H})-ones and studied their AMPA antagonistic activity.

Heinrich and coworkers\textsuperscript{223} in 1997, synthesized some substituted quinazolines and studied their NPY receptor antagonistic activity.

Elliot Mark and coworkers\textsuperscript{224} in 1997, prepared some 2,3-disubstituted quinazolin-4(3\textit{H})-ones. These compounds were found to possess AMPA receptor antagonistic activity.

In 1997, Sarac and coworkers\textsuperscript{225} described the synthesis of 4-aryl-1,2,3,4,5,6,7,8-octahydroquinazolin-2-thione derivatives.

Mitskyavichyus\textsuperscript{226} in 1997, synthesized certain analogs of 1-(2-carboxy ethyl) quinazolin-2,4-diones.

Arpad and coworkers\textsuperscript{227} in 1997, reported the synthesis of some fused heterocyclic quinazolin-4(3\textit{H})-ones.

Debi Prasad and coworkers\textsuperscript{228} in 1997, reported the synthesis of 2,3-disubstituted quinazolin-4(3\textit{H})-ones from acylamino-\textit{N}-arylbenzamides.

Aleem and coworkers\textsuperscript{229} in 1997, reported the synthesized some non-classical 2-amino-5,7-disubstituted tetrahydro
quinazolin-4-ones (151) and studied their thymidylate synthetase inhibition activity.

Monica and coworkers in 1997, described the stereoselective synthesis of 2,3-disubstituted-5-pyrrolidinone derivatives of quinazolin-4(3H)-ones.

Stefan Stankovsky and coworkers in 1997, described the synthesis of condensed quinazolines from 3-aryl-4-quinazolones.

Kalinowska and coworkers in the same year reported the synthesis of substituted quinazolin-4(3H)-ones (152).

Michael and coworkers in 1997, synthesized some 4-(anilino), 4-(phenoxy), 4-(thiophenoxy)-6,7-dimethoxy quinazolines (153).

Kazuyoshi and coworkers in 1997, described the synthesis of imidazo[3,4-a] quinazolinones (154).
In the same year, Volovenko\textsuperscript{235} described the synthesis of 6-substituted-2-cyano methyl quinazolin-4(3\textit{H})-ones (155).

Spirkova and coworkers\textsuperscript{236} in the same year, reported the synthesis of a series of 1,2,4-triazolo quinazolines (156).

Bertrand and coworkers\textsuperscript{237} in the same year, prepared a series of 3-phenyl/pyridyl-6-substituted quinazolin-4(3\textit{H})-ones. These compounds were reported to possess AMPA antagonistic activity.

Yong Chul and coworkers\textsuperscript{238} in 1998, prepared some substituted-1,3,4-triazoloquinazolines (157). These compounds were found to exhibit adenosine antagonistic activity.
Willard and coworkers\textsuperscript{239} in the same year, prepared a series of 3-phenyl-2,6-disubstituted quinazolin-4(3\textit{H})-ones \textbf{(158)} and studied their AMPA receptor antagonistic activity.

In 1998, Huang Charles and coworkers\textsuperscript{240} synthesized some 2,4,8-trisubstituted quinazolines \textbf{(159)}.

Yasser and coworkers\textsuperscript{241} in 1998, described the chemical transformations of 2,3-disubstituted-1,2,3,4-tetrahydro quinazolin-4-ones \textbf{(160)}.

Althebeiti and coworkers\textsuperscript{242} in 1998, reported the synthesis of some novel spirothiazolidinone and spiroazitidinone derivatives incorporated with quinazolines.

Du Jong and coworkers\textsuperscript{243} in 1998, described the synthesis of a series of 5-substituted quinazoline derivatives.
Shaban and coworkers\textsuperscript{244} in 1998, reported the synthesis of some 1,2,4-triazino[4,3-c] quinazolines and 4-(pyrazol-1-yl) quinazolines. In 1998, EL Deen and coworkers\textsuperscript{245} described the synthesis of 3-substituted-2-phenylamino-4-oxo quinazolines (161).

Mekuskiene and coworkers\textsuperscript{246} in 1998, synthesized some 2,3-disubstituted quinazolin-4(3\textit{H})-ones (162) and studied their mono amino oxidase inhibition activity.
Zohry and coworkers\textsuperscript{247} in 1998, reported the synthesis of spiroquinazoline-4-heterocyclic derivatives.

Feky and coworkers\textsuperscript{248} in 1998, reported the synthesis of some novel 2-substituted-3-aryl quinazolin-4(3\textit{H})-ones (163) from 2-cyano methyl-3-substituted phenyl-4(3\textit{H})-quinazolinone.

Robert and coworkers\textsuperscript{249} in 1998, reported synthesis of some 3-acetoxy amino quinazolin-4(3\textit{H})-ones.

S. Wojciech and coworkers\textsuperscript{250} in 1998, reported the synthesis of certain analogs of 4-substituted arylamino quinazolines (164) from 2-amino-\textit{N}-arylbenzamidines.
W. Wojciech and coworkers\textsuperscript{251} in 1998, reported the synthesis of certain analogs of 2,4-diamino quinazolinones.

Thierry and coworkers\textsuperscript{252} in 1998, reported the synthesis of 2-cyano-4-alkoxy-6,7-dimethoxy quinazolines (165).

Li Huiying and coworkers\textsuperscript{253} in 1998, reported the synthesis of some 4-quinazolinone oxime ethers (166).

Nilgun and coworkers\textsuperscript{254} in 1998, reported the synthesis of cyclohexylidene hydrazide derivatives of 3-phenyl-4(3\(H\))-quinazolinones (167).

In the same year Amine and coworkers\textsuperscript{255} described the synthesis of condensed quinazoline thiones (168).
In 1998, Tonkikh and coworkers\textsuperscript{256} reported the synthesis of certain analogs of 5,6,7,8-tetrahydro quinazolines.

Pastors and coworkers\textsuperscript{257} in 1998, described the synthesis of some 2-(trifluoromethyl)-3-substituted-4-oxo quinazolines (169) from 3-amino-2-(trifluoro methyl) quinazoline.

In 1998, Kandeel and coworkers reported\textsuperscript{258} the synthesis of substituted benzimidazolo, triazolo, tetrazolo and thiadiazolo quinazolines.

Ibrahim and coworkers\textsuperscript{259} in 1998, described the synthesis of some 3-substituted amino-2-methyl-4-oxo quinazolines (170).
Marcicatherine and coworkers\textsuperscript{260} in 1999, synthesized some 2-(substituted amino)-3-(alkoxyl phenyl) quinazolin-4(3\textit{H})-ones \textbf{(171)}. When tested for their biological activity, these compounds showed oestrogen agonistic activity.

In 1999, Pramila and coworkers\textsuperscript{261} prepared a series of 3-(substituted methyl)-2,6-disubstituted quinazolin-4(3\textit{H})-ones \textbf{(172)} and studied their antiamoebic activity. These compounds were found to exhibit good antiamoebic activity.

\begin{figure}
\includegraphics[width=\textwidth]{images/171_172.png}
\caption{Structures of compounds 171 and 172}
\end{figure}

Mateo and coworkers\textsuperscript{262} in 1999, described the intramolecular aza-witting reaction of imino-phosphoranes with \textbeta -lactam carbonyl group of substituted quinazolin-4-ones.

Mohammed Sadegh and coworkers\textsuperscript{263} in 1999, reported the microwave promoted synthesis of substituted quinazolin-4-(3\textit{H})-ones.
Feng and coworkers\textsuperscript{264} in 1999 described the rearrangement of 4-imino benzoazines to 4-quinazolinones via amidine carboxamides.

Santagati and coworkers\textsuperscript{265} in 1999 described the new synthetic approaches to fused heterocyclo quinazolones (173).

Xuedong and coworkers\textsuperscript{266} in 1999, reported the synthesis of 2-substituted quinazolinones.

Kawadkar and coworkers\textsuperscript{267} in 1999, described the synthesis of some novel substituted quinazolin-4-ones.

Keith and coworkers\textsuperscript{268} in 1999, described the synthesis of 2-substituted quinazolin-4(3\textsubscript{H})-ones (174).

Laurent and coworkers\textsuperscript{269} in 1999, reported the synthesis of a series of oxindole quinazolines.
Reddy and coworkers\textsuperscript{270} in 1999, reported the synthesis of some 2-substituted quinazolin-4(3\textit{H})-ones.

In 1999, Bharadwaj and coworkers\textsuperscript{271} reported the synthesis of some substituted pyrido quinazolines (175).

Bahekar and coworkers\textsuperscript{272} in 1999, described the synthesis of some novel benzimidazo[1,2-\textit{c}] quinazolin-6(5\textit{H})-ones (176).

Mohammed and coworkers\textsuperscript{273} in the same year, reported the synthesis of 6-substituted benzimidazo[1,2-\textit{c}]quinazolines under microwave irradiation.

Ji Wang and coworkers\textsuperscript{274} in 1999, described the synthesis of 3-(substituted biphenyl)-2-substituted quinazolin-4(3\textit{H})-ones (177). The pharmacological investigation of these compounds showed angiotensin-II antagonistic activity.

Jorg and coworkers\textsuperscript{275} in 1999, reported the synthesis of some substituted 4-oxo quinazolines.
Tombary and coworkers\textsuperscript{276} in 1999, reported the synthesis of some novel triazolo[4,3-\textit{a}]quinazolines and bistriazolo[4,3-\textit{a}]quinazolines.

Mamoru and coworkers\textsuperscript{277} in 1999, described the thermal ring contraction of 1,4-benzodiazepines into quinazolines.

Sharma and coworkers\textsuperscript{278} in 1999, reported the synthesis of 7,8,9,10-tetrahydroazepino[2,1-\textit{b}]quinazolines. These compounds were found to possess bronchodilator activity.

Spirkova and coworkers\textsuperscript{279} in 1999, reported the synthesis of some 2-morpholino methyl-3-substituted quinazolin-4(3\textit{H})-ones \textbf{(178)}.

In 1999, Mohammed and coworkers\textsuperscript{280} reported the synthesis of 2-phenyl-3-substituted-4-oxo quinazolines \textbf{(179)}. 
Strakov and coworkers\textsuperscript{281} in 1999, reported the synthesis of 3-(6-amino-2-pyridyl)-2-methyl-4(3\textit{H})-quinazolinone (180) and its chemical reactions.

In 1999, Ramana and coworkers\textsuperscript{282} described the synthesis of 2-substituted quinazolin-4(3\textit{H})-ones (181).

Abderrahim and coworkers\textsuperscript{283} in 1999, reported the synthesis of certain analogs of substituted triazolo quinazolines (182).

Pfeiffer and coworkers\textsuperscript{284} in 1999, reported the synthesis of some substituted-1,2,4-triazolo quinazolines.
In 2000, L. Bertelli and coworkers\textsuperscript{285} synthesized substituted 1,2,3-triazolo[1,5-a] quinazolines and reported their binding affinity towards benzodiazepine and adenosine receptors.

Lucia and coworkers\textsuperscript{286} in 2000, prepared some 1,2,3-triazolo quinazolines. Biological investigation of these compounds showed adenosine and benzodiazepine receptor agonistic activity.

In the same year, Noriko and coworkers\textsuperscript{287} synthesized some 1-methyl-4-(3-substitutedpropyl)-7,8-disubstituted-1,2,4-triazolo quinazolin-4(3\$H\$)-ones (183) and studied their enzyme inhibition activity.

![Chemical structures](image)

In 2000, Szczepankiewicz and coworkers\textsuperscript{288} reported the synthesis of some novel 3-(2-cyano phenyl) quinazolin-4(3\$H\$)-ones.
The above same workers\textsuperscript{289} in 2000, also reported the synthesis of 4-arylamino quinazolines and 2-aryl-4-arylaminoquinazolines.

Patel and coworkers\textsuperscript{290} in 2000, reported the synthesis of 2-methyl-3-(2-methyl phenyl)-6-arylazo quinazolin-4-one and its derivatives.

Pavel and coworkers\textsuperscript{291} in the same year, reported the synthesis of some 2-phenyl-2-hydroxy methyl-4-oxo-1,2,3,4-tetrahydro quinazoline and its derivatives.

In 2000, Ali Hussain and coworkers\textsuperscript{292} reported the synthesis of o-ethyl phosphorodiamidates from substituted quinazolin-4-ones.

Aleem and coworkers\textsuperscript{293} in 2000, synthesized a series of novel non-classical reversed bridge quinazolines and studied their thymidylate synthetase inhibition activity.

Abdugafurov and coworkers\textsuperscript{294} in 2000, reported the synthesis of 3-(substituted triazolo methyl)-2-alkyl-4-oxo quinazoline (184) derivatives.

Benedict and coworkers\textsuperscript{295} in 2000, prepared some 2-substituted amino quinazolin-4-ones and studied their biological activity. These compounds were found to be potassium channel openers.
In 2000, Petra and coworkers\textsuperscript{296} reported the synthesis of 5,6,7,8-tetrahydro-2,6-diamino quinazolines.

Witt and coworkers\textsuperscript{297} in 2000, prepared a series of 2-vinyl-3\textit{H}-quinazolin-4-ones and studied their chemical reactions.

In the same year, Simon and coworkers\textsuperscript{298} described the synthesis of some 2-substituted aryl quinazolin-4(3\textit{H})-ones.

Hiti and coworkers\textsuperscript{299} in 2000, reported the synthesis of some substituted quinazolin-4(3\textit{H})-ones.

Helmuth and coworkers\textsuperscript{300} in the same year studied a novel isocyanate reaction on quinazolines (185) in which the formation of unexpected cycloadducts was observed.

![Chemical structures](184) \hspace{1cm} (185)

In 2000, Muijlwijk-Koezen and coworkers\textsuperscript{301} synthesized a series of substituted quinazolines and studied their human adenosine A\textsubscript{3} receptor antagonistic activity.
Julio and coworkers$^{302}$ in 2000, reported the microwave enhanced synthesis of 2-(2-amino phenyl)-4-amino quinazoline derivatives (186).

Ding ming and coworkers$^{303}$ in 2000, described the synthesis of 2-substituted amino-3-(substituted phenyl) quinazolin-4(3$H$)-ones (187).

![Chemical structures (186) and (187)](image)

Jun Min and coworkers$^{304}$ in 2000, prepared some $\alpha$-thiocarbonyl phosphoric acid derivatives of quinazoline analogs.

Hiyoshizo and coworkers$^{305}$ in 2000, reported the synthesis of some substituted quinazolines.

Azizian and coworkers$^{306}$ in 2000, described the rearrangement of 4-imino(1$H,4H$)-3,1-benzoxazine-2-ones to quinazolin-2-4-diones.

Tonkikh and coworkers$^{307}$ in the same year synthesized some 2-substituted-5-oxo-5,6,7,8-tetrahydro quinazolines.
Sahadeva and coworkers\textsuperscript{308} in 2000, synthesized a series of substituted indolyl quinazolines.

Takumi and coworkers\textsuperscript{309} in 2000, described the synthesis of substituted quinazolines using carbon dioxide (or) carbon monoxide with sulfur under mild condition.

Wojciech and coworkers\textsuperscript{310} in 2000, reported the synthesis of 4-amino-2-phenyl quinazoline and its derivatives.

Cyril and coworkers\textsuperscript{311} in 2000, described the synthesis of some 5-chloro-2-methyl-3-(5-methylthiazol-2-yl)-4(3\textit{H})-quinazolone derivatives and studied their biological activities.

Srivastava and coworkers\textsuperscript{312} in 2000, reported the synthesis of 3-substituted amino-2-alkyl/aryl-4-oxo quinazolines (188).

In 2002, F. Varano\textsuperscript{313} et. al., synthesized a new set of pyrazolo[1,5-c]quinazoline-2-carboxylates and evaluated their excitatory amino acid antagonistic activity.

In 2003, V. Colotta\textsuperscript{314} et. al., synthesized 4-amino-6-(hetero)arylalkylamino-1,2,4-triazolo[4,3-a]quinoxalin-1-one derivatives and reported that these compounds showed a potent A(2A) adenosine receptor antagonists.
In 2003, Reddy and coworkers\textsuperscript{315} synthesized some new 4-aryl-1,2,4-oxadiazino[5,4-\textit{b}]quinazolines (189) from 2-chloro quinazolin-4-one.

![Chemical structures of compounds 188 and 189](image_url)

In 2003, Gangual and coworkers\textsuperscript{316} prepared some 1,2-disubstituted quinazolines (190).

In the same year Reddy and coworkers\textsuperscript{317} reported the synthesis of some bismethaqualone, bismecloqualone and bispiroqualone analogues.

Kant and coworkers\textsuperscript{318} in 2003, prepared a series of 2,3-disubstituted quinazolines (191).

![Chemical structures of compounds 190 and 191](image_url)
In 2007, C. Balo and coworkers synthesized a series of [1,2,4] triazolo[1,5-c]quinazolines and these compounds were screened for their adenosine antagonistic activity.

In 2010 Selvam et. al., synthesized a novel 6, 7, 8, 9-tetrahydro-5H-5-phenyl-2-benzylidine-3-substituted hydrazino thiazolo(2,3-b)quinazoline derivatives and screened for anthelmintic activity.

Saravanan and coworkers in 2010, reported a novel quinazolinone derivatives which showed more potent antioxidant activity.