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A REVIEW ON SYNTHESIS AND BIOLOGICAL ACTIVITY OF SOME NOVEL QUINAZOLINONE AND QUINAZOLINONE-THIAZOLIDINE DERIVATIVES

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ABSTRACT

In several new classes of structurally quinazolinones and quinazolinone-thiazolidines compounds were synthesized in the study of the current literature. 3-amino-2-methylquinazolin 4(3*H*)-one was synthesized from anthranilic acid through 2-methylbenzoxazin-4-one. The present literature of the Journal for the study of the synthesis of quinazolinones and quinazolinone-thiazolidines compounds and their derivatives that have specific pharmacological and biological activity such as antimicrobial, antibacterial, antifungal, antiviral, antispasmodic, anti-inflammatory, antihistamine, anticancer activity, etc.

KEYWORDS: Biological activity, Quinazolinone, Quinazolinone-thiazolidines compounds.

1. INTRODUCTION

In recent years, quinazolin4(3*H*)-one have become increasingly important in chemistry due to their biological importance. A derivative of quinazolin4one with a wide range of biological and pharmacological activities. The compounds of quinazolinones and quinazolinone- thiazolidines are notable in medical chemistry because those of quinazolin 4(3*H*)-one have been reported to have a wide range of biological activities such as anti-microbial, anti-tubercular, anti-malarial, analgesic, anti-inflammatory, anti-convulsant, anti-cancer, and anti-viral activities.[1]

Quinazoline derivatives represent one of the most active classes of compounds that have a wide range of biological activity. They are widely used in pharmaceutical and agrochemical products, for example, fluquinconazole fungicide used to control agricultural diseases. Several reports have been published on the biological activity of quinazoline derivatives, including their bactericidal, herbal, and antitumor activities.[2]

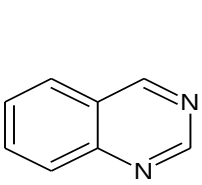
1.1 Chemistry of quinazoline

In 1903 Gabriel turned into first discovered that quinazoline in laboratory. Quinazoline is an fragrant heterocyclic compound with the components C8H6N2. It is a bicyclic shape compound organized through fused six-membered easy fragrant rings-benzene and pyrimidine ring. The homes of the pyrimidine ring have been laid low with the prevalence of fused benzene ring. The nitrogen atoms aren't different, and the awesome polarization of the 3,4-double bond is meditated withinside the reactions of quinazoline.

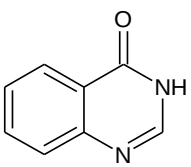
Quinazoline is a heterocyclic molecule made up of two simple aromatic rings with six members each: benzene and pyrimidine. It's a yellow-coloured chemical that usually starts out as a crystalline form. Quinazolinones will be divided into the following five groups based on their ring system substitution patterns.

1) 2-substituted-4(3H)-quinazolinones,
2) 3-substituted-4(3H)-quinazolinones,
3) 2,3-disubstituted-4(3H)-quinazolinones,
4) 2,4-disubstituted-4(3H)-quinazolinones, and
5) 4-substituted-4(3H)-quinazolines

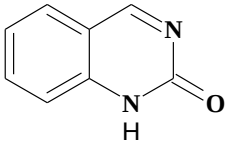
According to the position and amount of carbonyl groups, these compounds can be categorised into three kinds based on the position of the keto or oxo group: 2(1H) quinazolinones, 4(3*H*) quinazolinones, and 2,4(1*H*,3*H*) quinazolinedione.[3]



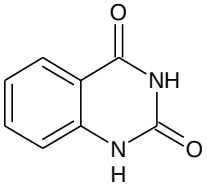
quinazoline



quinazolin-4(3*H*)-one



quinazolin-2(1*H*)-one



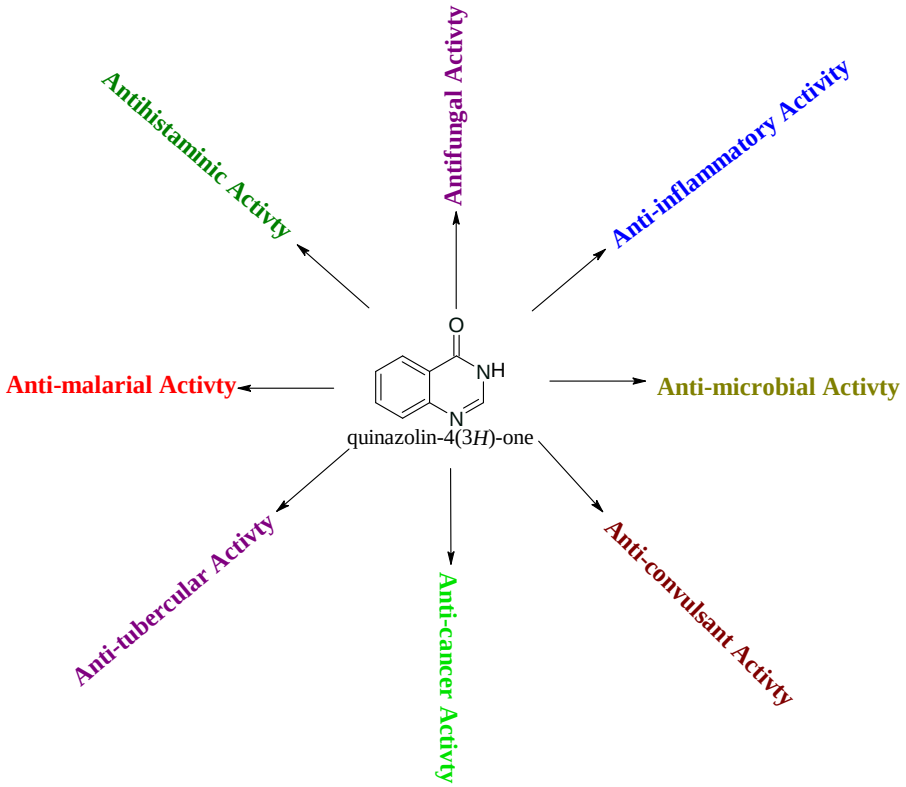
quinazoline-2,4(1*H*,3*H*)-dione

Anthranilic acid was treated with acetic anhydride to produce 2-methyl benzoxazin-4-one, which was then reacted with hydrazine hydrate to produce 3-amino-2-methyl quinazolin-4-(3*H*)-one. Compound 3 was used to generate schiff bases by reacting with different aromatic aldehydes in the presence of ethanol as a solvent.[4]

1.2 Biological importance of quinazolinones

This review is a challenge to increase the huge potentiality and resolute on the various biological activities of quinazolinones and quinazolinone-thiazolidine compounds.

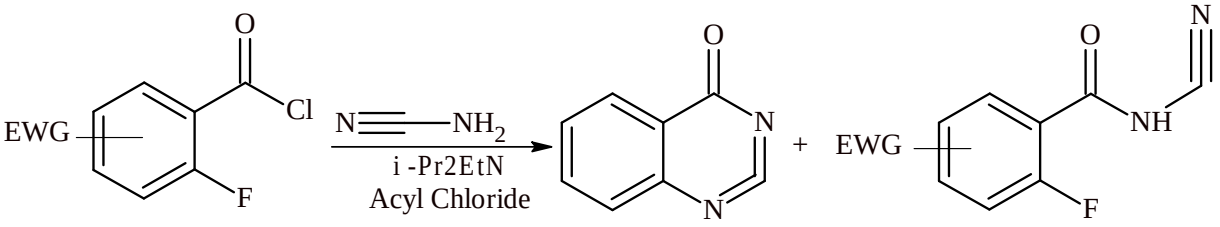
The backbone of quinazolinone is a heterocycle often found in the literature of medicinal chemistry with applications such as antibacterial, analgesic, anti-inflammatory, antifungal, antimalarial, CNS depressant, anticonvulsant, anticoccidial, antiparkinsonian, and caner activities.[5]



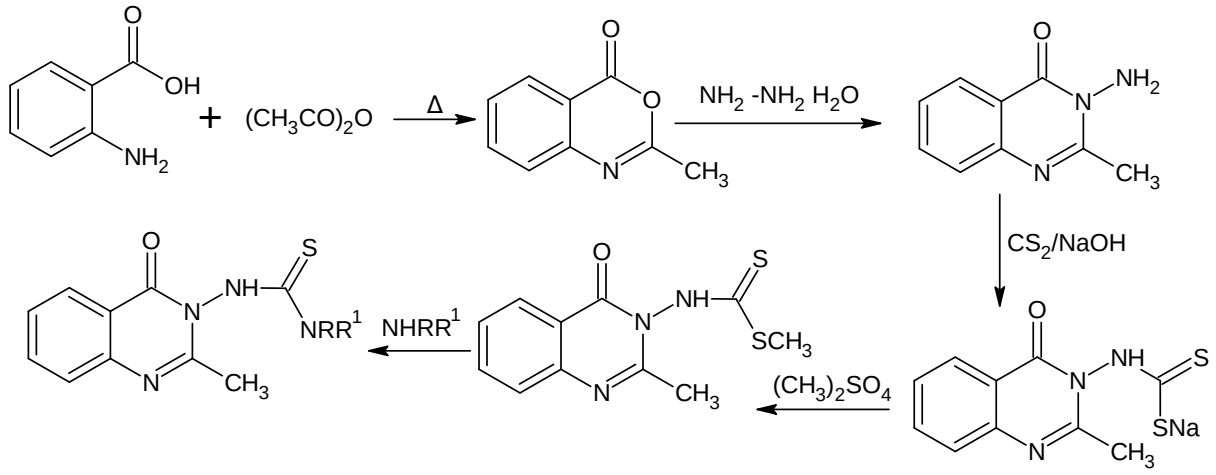
2. METHODS AND SYNTHESIS

2.1 Different schemes for synthesis of Quinazolin-4(3*H*)-ones

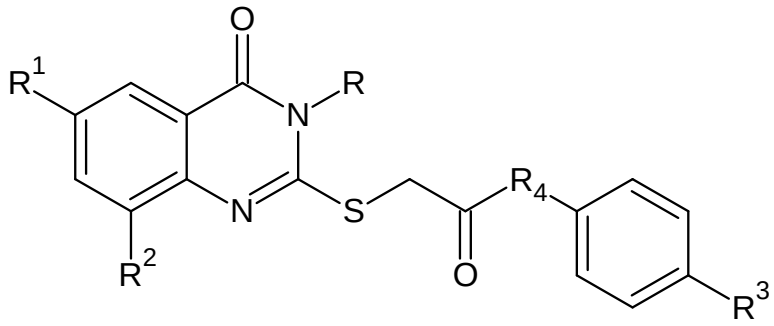
Martin J *et al*., (2001) were reported synthesized 4(3*H*)-quinazolinones from 2-Fluoro substituted benzoyl chlorides with 2-amino-*N*-heterocycles by cyclo-condensation reaction. The reaction profits reasonable yields with a various combinations of benzoyl chloride and 2-amino-*N*-heterocycles.[6]



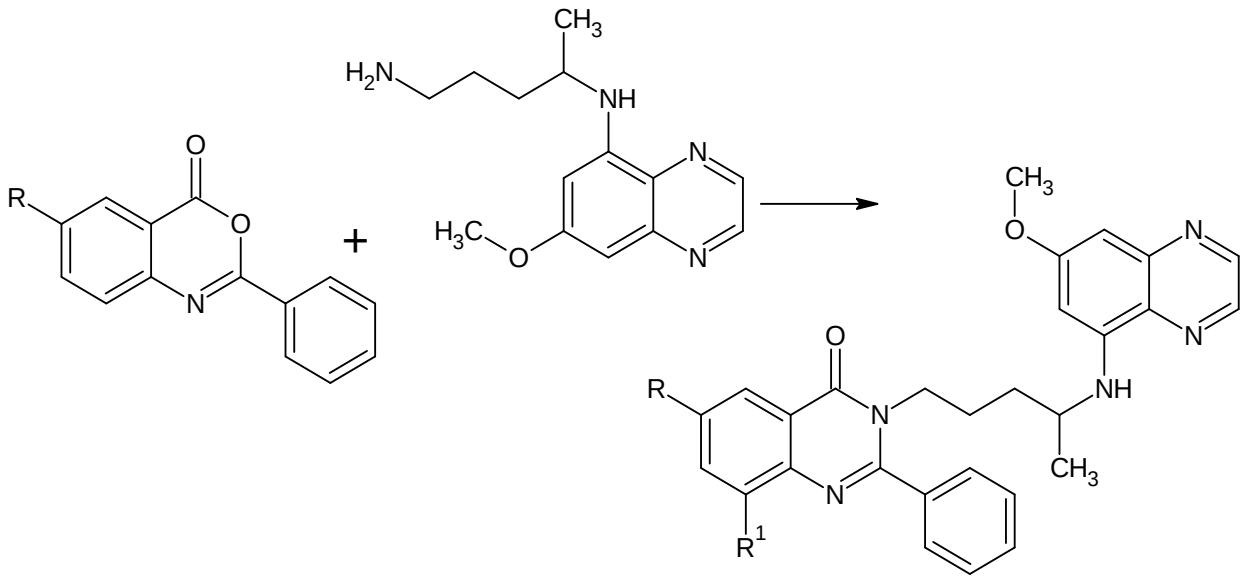
Veerachamy Alagarsamy, *et al*., (2003) were reported Synthesis, Analgesic, Anti-inflammatory and Antibacterial Activities of Some Novel 2-Methyl-3-substituted Quinazolin-4-(3H)-ones.[7]



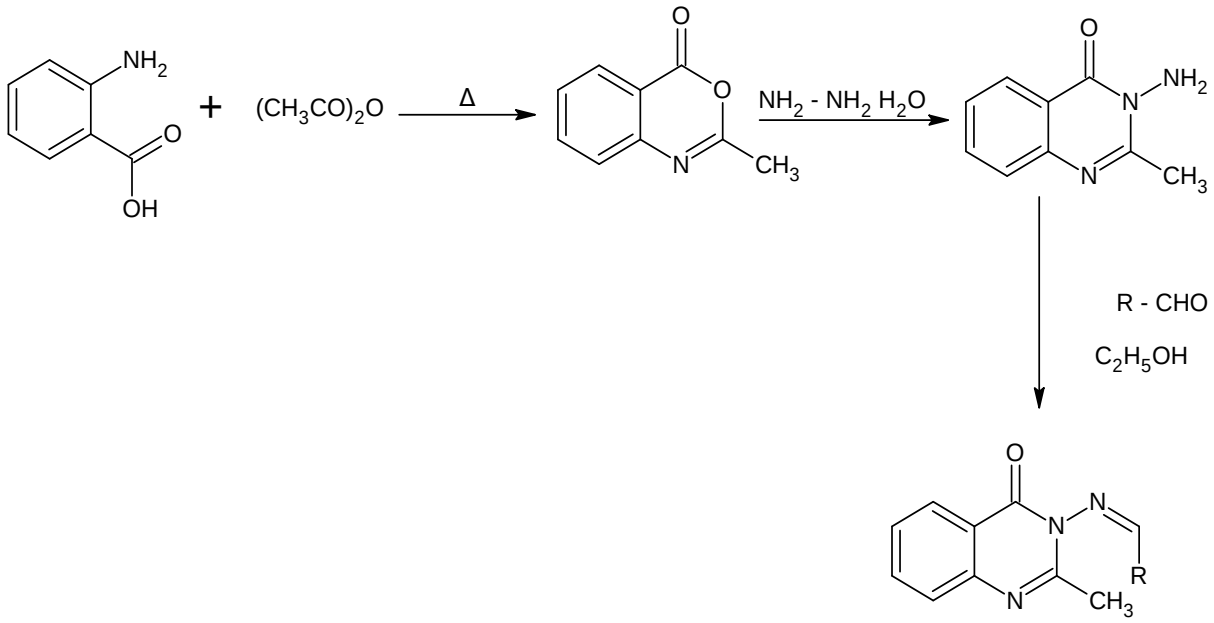
Abdel Ghany Aly El-Helby *et al*., (2003) were reported synthesized a novel series of 3-substituted(methyl, ethyl or phenyl)-3*H*-quinazolin-4-one. The newly produced compounds showed promising antiepileptic activity and Phenobarbitone sodium was a standard.[8]



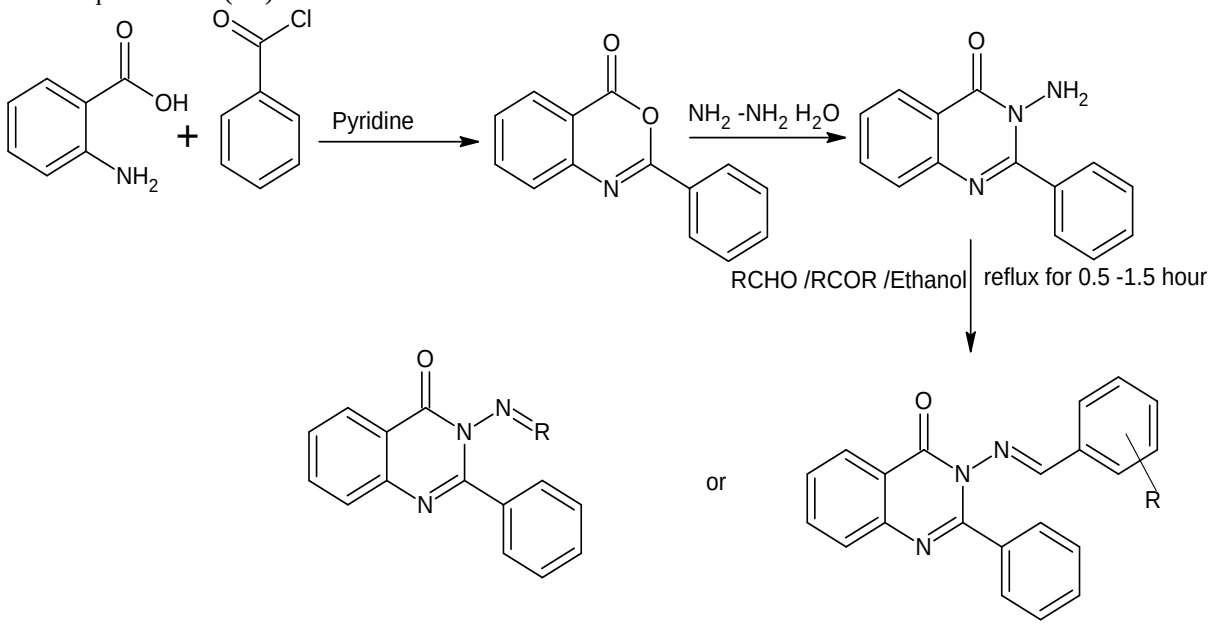
P. SELVA *et al*., (2008) were reported synthesized new sequence of 2, 3-disubstituted quinazolin- 4(3H)-one. Synthesized compounds had in vitro antiviral activity.[9]



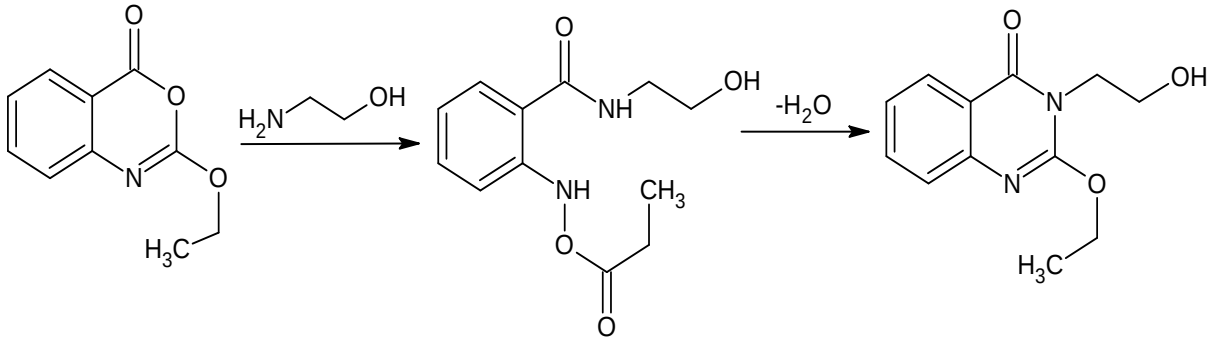
Govindaraj Saravanan* *et al*., (2010) were reported Synthesis, analgesic and anti-inflammatory screening of novel Schiff bases of 3-amino-2-methylquinazolin-4-(3*H*)-one.[10]



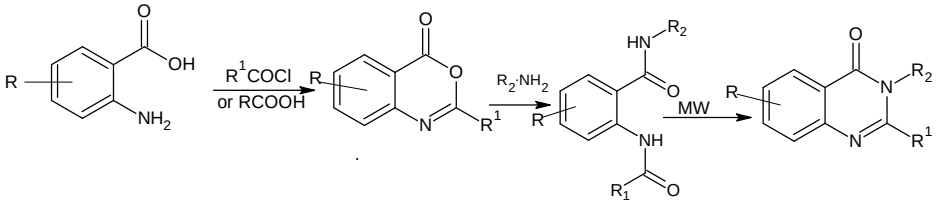
S.K. KRISHNAN, *et al*., (2011) were reported Synthesis, antiviral and cytotoxic investigation of 2-phenyl-3-substituted quinazolin-4(3H)-ones.[11]



Maher A. El-Hashash *et al*., (2011) were reported Synthesized 2-ethoxy-(4*H*)-3,1-benzoxazin-4-one derivatives and found potential antimicrobial activity.[12]

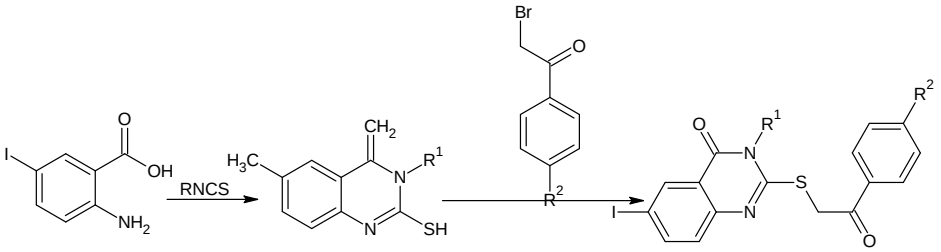


D.A. Patil *et al.*, (2011) were reported synthesized of bioactive 2, 3-disubstituted-quinazoline-4(3*H*) - one compounds.[13]



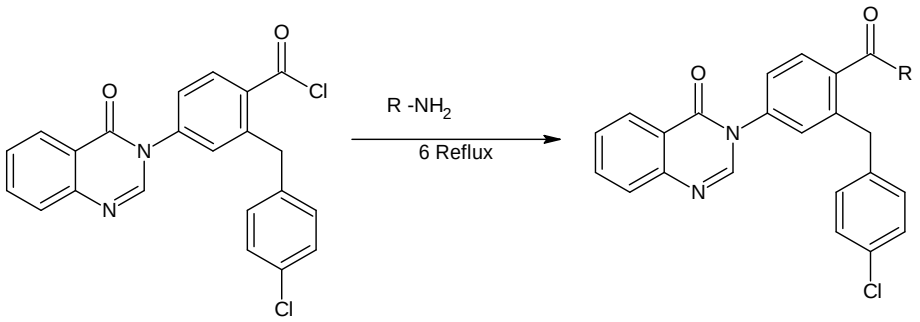
R=5-CH3, 4, 5-(OCH3)24-Cl, H. R1=Me, Et, R2=Bn, Ph, etc.

Ahmed Mahmoud Alafeefy *et al*., (2011) were reported series of some latest 2, 3-disubstituted- 6-iodo-3H-quinazolin-4-one derivatives. The cytotoxic outcomes were obtained with compounds having allyl and/or benzyl molecule at positions 2 and/or 3 at quinazoline nucleus had better antitumor activity than the standard drug Doxorubicin.[14]

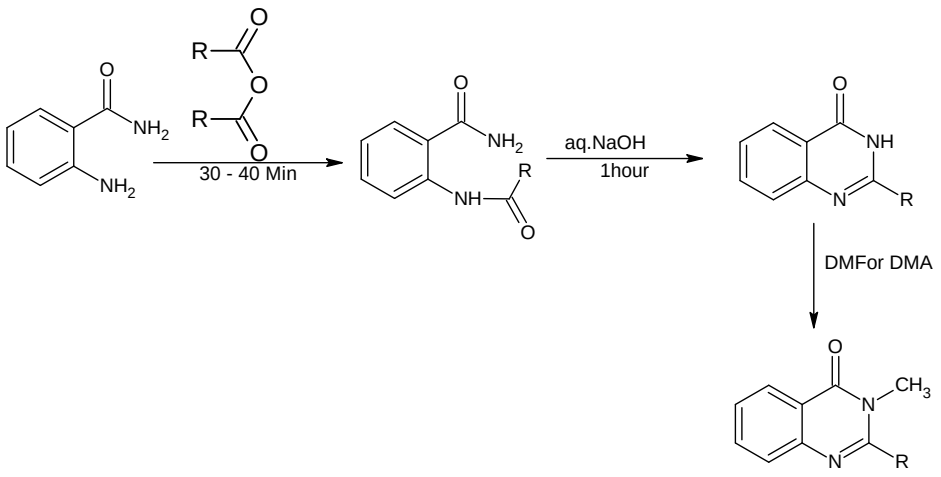


R and R^1 allyl, Benzyl. R^2- HCl NO_2

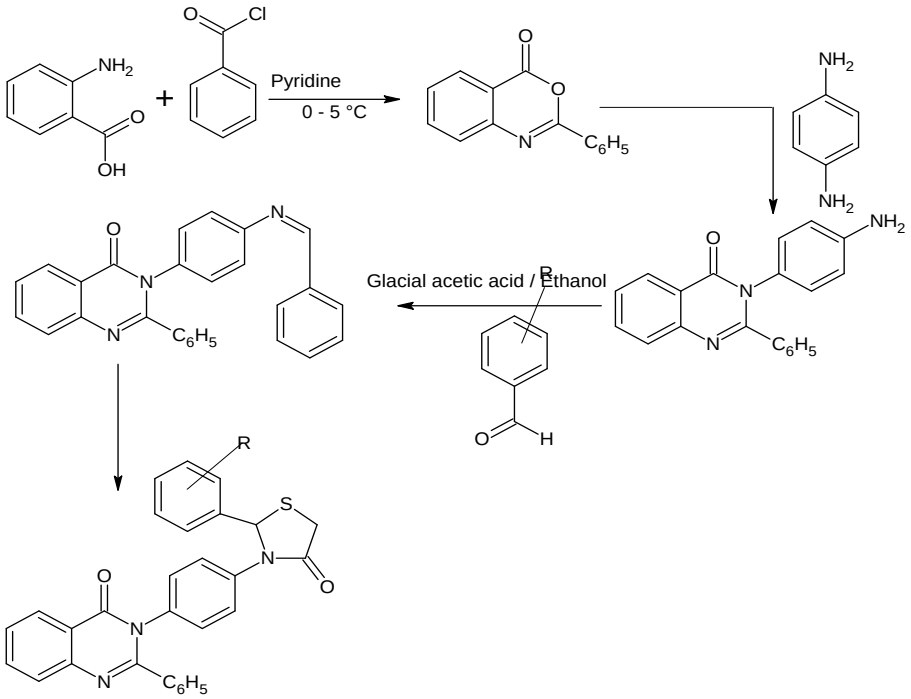
Hurmath Unnissa *et al*., (2013) were reported Synthesized sequence of 4-[2-(4-chlorobenzyl)-4-oxoquinazolin-3(4H)-yl) benzoyl]. The sequence exhibited significant Antioxidant and Antitumor activities.[15]



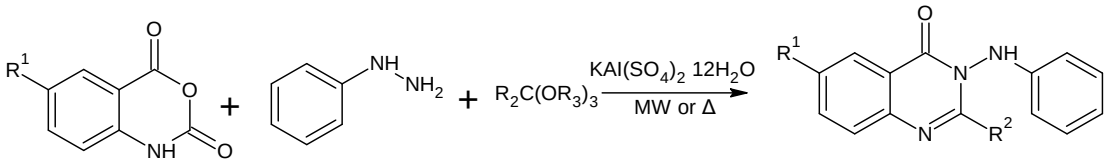
Mohammad Rafeeq *et al*., (2015) were reported evaluated the potential of N, N-dimethyl formamide dimethyl acetyl (DMF-DMA) as a methylating substance which was used for the reactions of 2-alkyl substituted quinazolin-4(3H)-one in solvent free condition.[16]



Samridhi Thakrall et *al*., (2017) were reported a synthetic approach and molecular docking study of hybrids of quinazolin-4-ones and thiazolidin-4-ones as anticancer agents.[17]

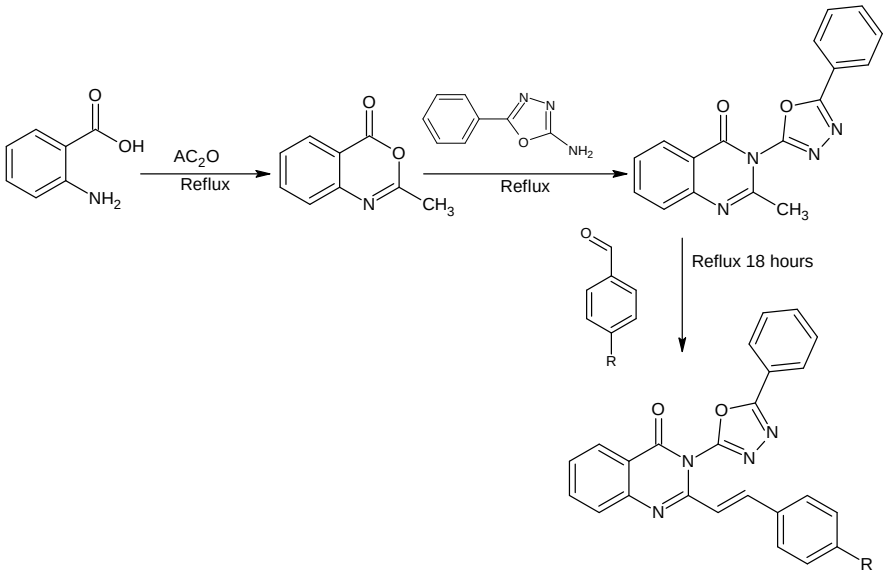


Ali Asghar Mohammadi *et al*., (2017) worked on microwave to synthesize of 2-Alkyl and 2-aryl-3-(phenylamino) quinazolin-4(3*H*)-ones. Derivatives, unsubstituted at position 2 of the quinazoline molecule showed plentiful antibacterial action compared to standard.[18]

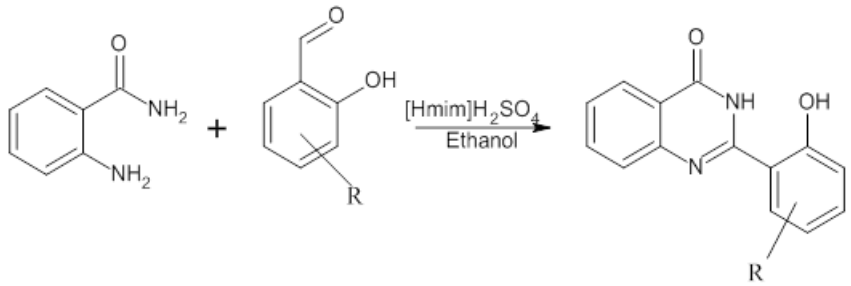


R1=H, Cl. R2=*n*Pr, Methanol. R3 =Ethanol, Methanol.

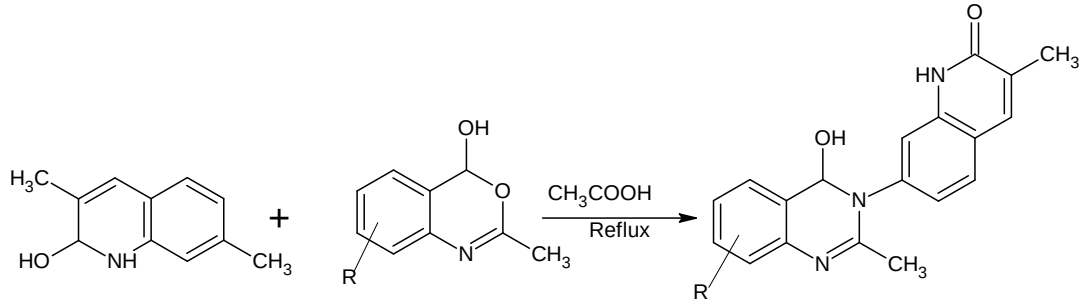
Sweta Garg *et al*., (2017) were reported synthesized di-substituted quinazoline-4(3H) one compounds with various aldehydes and assessed their activity against microbial and inflammatory conditions.[19]



Suresh C Jadhvar *et al*., (2017) were reported synthesized 2-(2-hydroxyaryl) quinazolin-4(3H)-one derivatives *via* reaction between *o*-amino benzamide and substituted salicylaldehyde using [Hmim] HSO4 as catalyst. The article showed that some synthesized derivatives presented noteworthy inhibition of human breast cancer cell lines compared with the reference drug.[20]

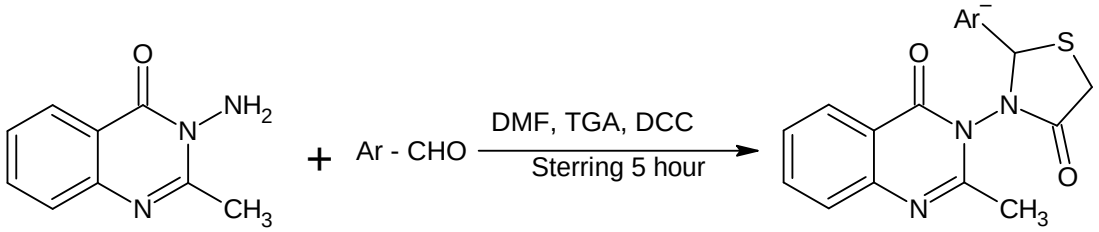


Santosh Kumar *et a*l., (2018) were reported di-substituted quinazolin-4(3H)-one derivatives.6,8-dibromo-2-methyl-3-(4-methyl-2-oxo-1,2-dihydroquinolin-7-yl) quinazolin-4(3H)-one and 2-methyl-3-(4-methyl-2-oxo-1,2-dihydroquinolin-7-yl)-7-nitroquinazolin-4(3H)- one showed the highest anti-inflammatory action in carrageen induced paw edema model.[21]



R=H, 6, 8-dibromo or 7-nitro

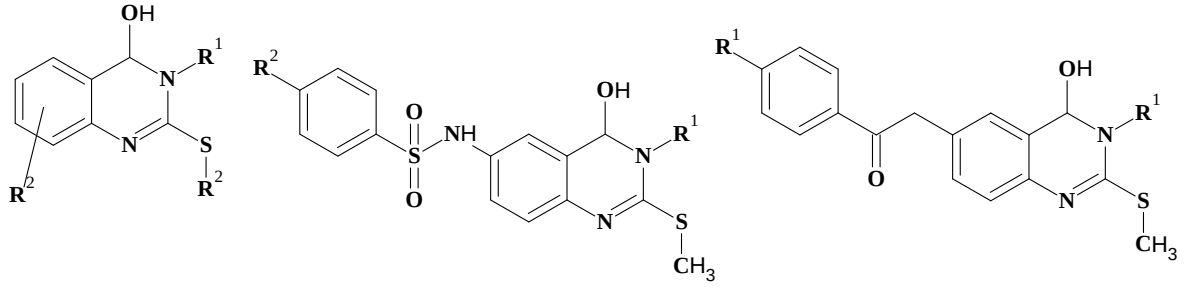
S. S. Jangama *et al*., (2019) were reported Synthesis, Molecular Docking, and Biological Evaluation of the New Hybrids of 4-Thiazolidinone and 4(3H)-Quinazolinone against Streptozotocin induced Diabetic Rats.[22]



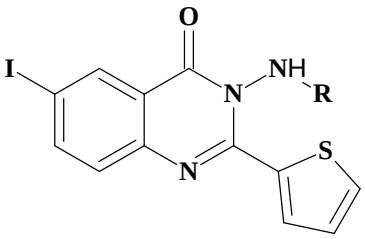
3. BIOLOGICAL IMPORTANCE

3.1 ANTICANCER ACTIVITY

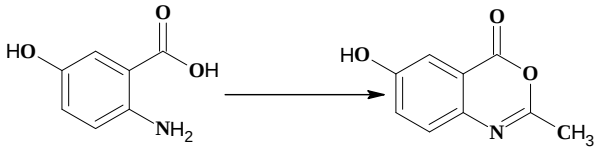
Sarah T *et al*., (2006) were reported a sequence of quinazoline analogs to look like methotrexate structure. The synthesized derivatives were evaluated for their capacity to reduce mammalian DHFR and for their antitumor activity.[23]



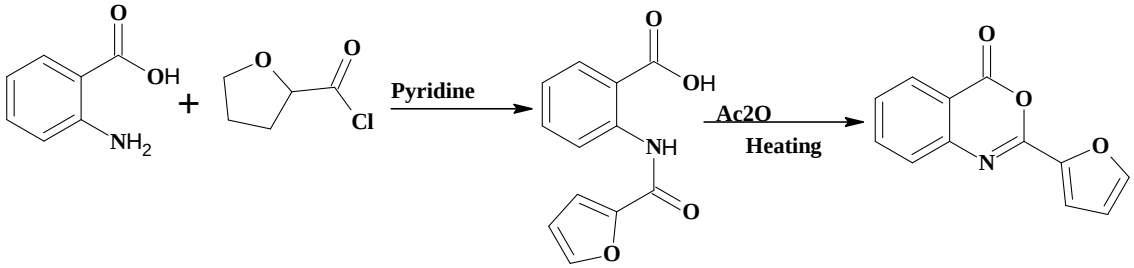
Abdulrahman M. Al-Obaid *et al*., (2009) were reported synthesized of some new 2-thieno-4(3H)-quinazolinone series and compared to the known drug 5-Fluorouracil. These quinazolinone sequence could be believed as helpful templates for potential development to achieve more prominent anticancer agents.[24]



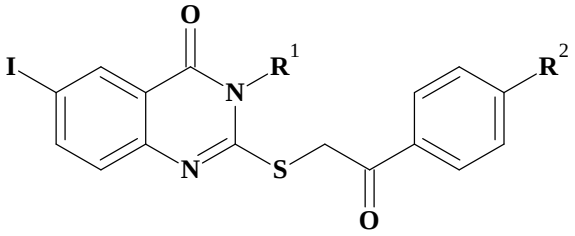
Ahmed Kamal *et al*., (2010) were reported Synthesis of benzoxazinone from condensation of 5-hydroxy anthranilic acid with acetic anhydride.[25]



Malleshappa N. Noolvi *et al*., (2011) were reported Synthesis of 2-(furan-2-yl)-4H-3, 1- benzoxazin-4-one by refluxing 2[(furan-2-yl carbonyl) amino] benzoic acid with acetic anhydride.[26]

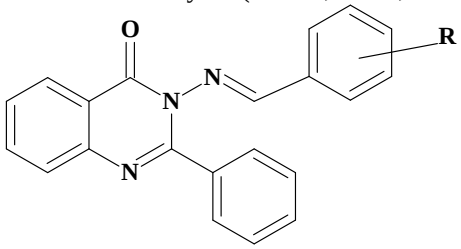


Ahmed Mahmoud Alafeefy *et al*., (2011) were reported some new quinazolin-4(3H)-one derivatives, synthesized and antitumor activity.[27]

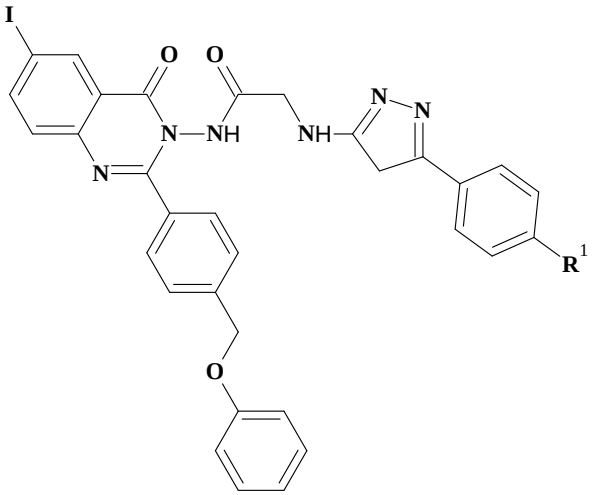


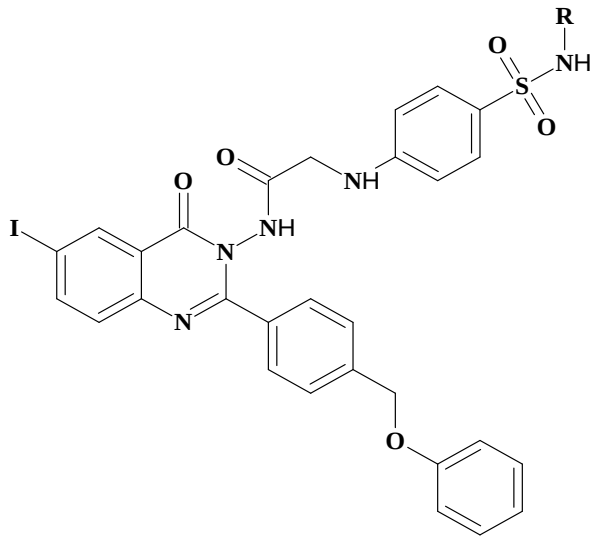
R^1=benzyl, R^2=Br. R^1=phenyl, R^2=Br. R^1=allyl, R^2=Cl .R^1=benzyl, R^2=Cl.
R^1=phenyl, R^2=Cl. R^1=allyl, R^2=NO_2. R^1=benzyl, R^2=NO_2.

Subhadip Das *et al*., (2012) were reported the evaluation of the antitumor activity of these quinazolinones.[28]
R=substituted benzaldehydes (3-NO2, 2-OH, 4-OCH3)



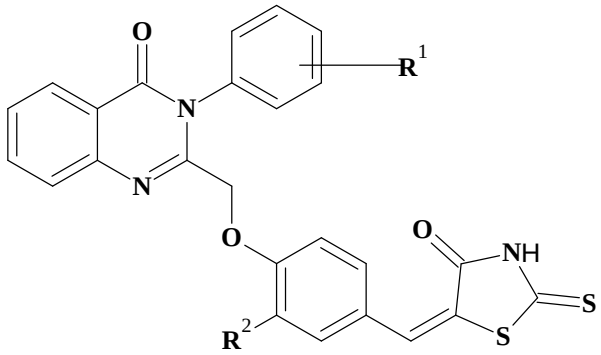
Safinaz E *et al*., (2013) were reported synthesized various derivatives of 6-iodo-2-phenoxymethyl 3-substituted quinazolin-4(3H)-ones. The in vitro antitumor activity of the synthesized compounds against breast cell line was carried out using Doxorubicin as a standard drug. Derivatives revealed a considerable activity.[29]



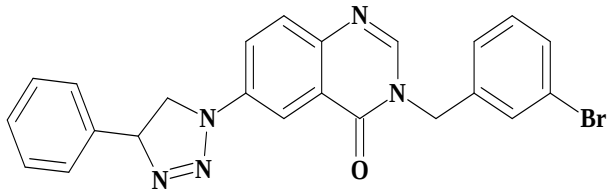


A=S or O and R1=Cl or H etc. R=C5H4N, C6H5 or H

Sherihan El-Sayed *et al*., (2017) were reported on Synthesis and anticancer activity of novel quinazolinone-based rhodanines.[30]

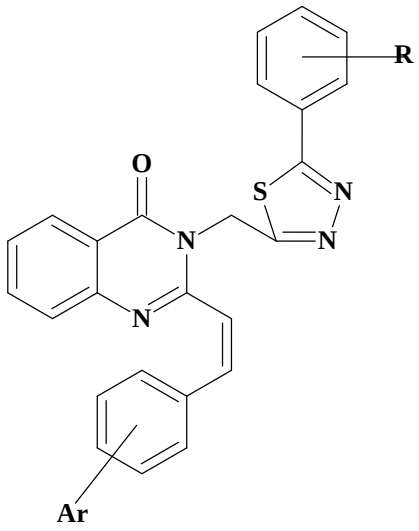


Srikanth Gatadi *et al*., (2020) were reported Synthesized a sequence of novel quinazolinones and estimated their cytotoxic activity against a various human cancer cell lines. They showed apoptosis, chromatin condensation and horseshoe shaped nuclei appearance.[31]

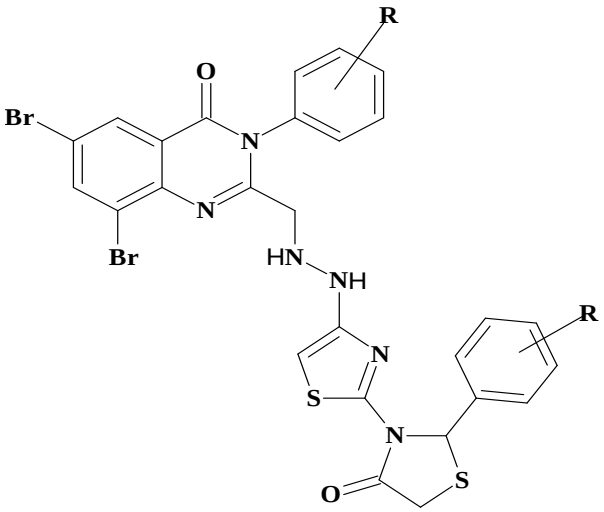


3.2 ANTICONVULSANT ACTIVITY

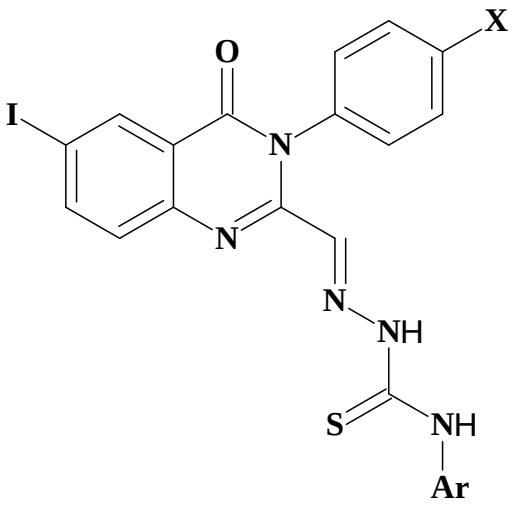
Shashikant V. Bhandari *et al*., (2008) were reported a variety of 3-[5-substituted 1, 3, 4- thiadiazol-yl]-2- styryl quinazolin-4(3H)-ones derivatives. Some of the synthesized derivatives showed considerable anticonvulsant activity similar to the standard Phenytoin, Diazepam and Phenobarbital.[32]



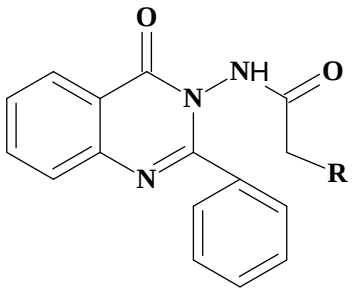
Neha Garg *et al*., (2009) were reported synthesized a novel analogs of 3-(4-(2-(6, 8-dibromo-3- (substituted phenyl)-4-oxo-3,4 dihydroquinazolin-2-yl)methyl) hydrazinyl)thiazol-2-yl)- 2-phenylthiazolidin-4-ones(I) and a few of its derivatives showed effective anticonvulsant activity.[33]



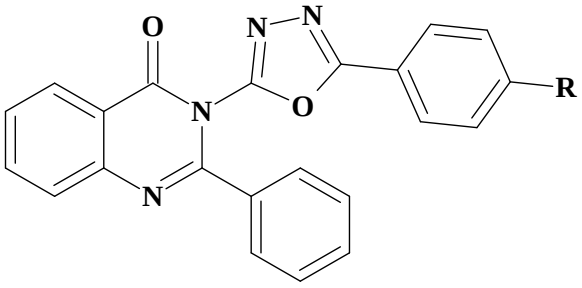
Mohsen M. Aly *et al*., (2010) were reported synthesized a 3-aryl-4(3*H*)-quinazolinone-2 carboxaldehydes. Screening for some chosen derivatives was carried out to explore their potential anticonvulsant, analgesic, cytotoxic as well as their antimicrobial activities.[34]



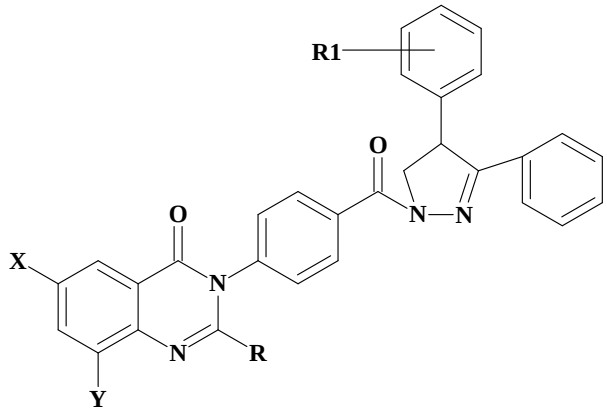
Rajasekaran S *et al.*, (2010) were reported synthesized antitubercular, antibacterial and antioxidant activity of some 2-phenyl-3-substituted quinazolin-4(3*H*)-ones.[35]



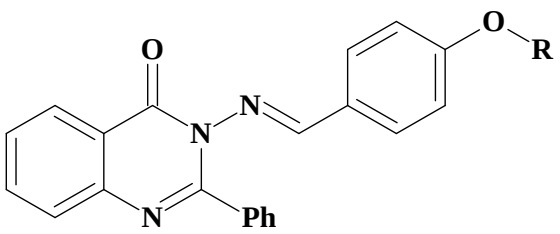
Anjali G *et al.*, (2011) were reported synthesized a series of 3-[5-(4-substituted) phenyl- 1,3,4- oxadiazole-2yl]-2 phenylquinazoline-4(3*H*)-ones. They were observed with moderate action in the maximum electric shock seizures and PTZ provoked seizure models in rats.[36]



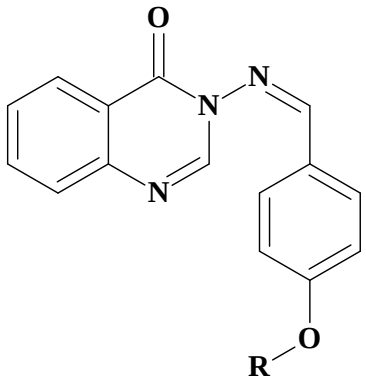
Veerachamy Alagarsamy and Govindaraj Saravanan *et al.*, (2013) were reported synthesized novel 6, 8- (dibromo/H)-2-(methyl/phenyl) 3-(4-(5-(substitutedphenyl)-3-phenyl-4, 5-dihydro-1H- pyrazole-1-carbonyl) phenyl)-4(3*H*) quinazolinone. The designed derivatives showed moderate anticonvulsant activity in maximal electric shock and subcutaneous pentylenetetrazole seizure induced tests.[37]



Mohd Amir et al (2013) were reported prepared a sequence of 3-[(4-substituted-benzylidene)-amino]- 2-phenyl-3H-quinazolin-4-ones. Anti-convulsant actions were screened by the maximal electric shock and subcutaneous Pentylenetetrazole. Compound 3-[(4-butoxy- benzylidene)-amino]-2-phenyl-3H-quinazolin-4-one was came out as the mainly capable anticonvulsant agent lacking any motor impairment result.[38]

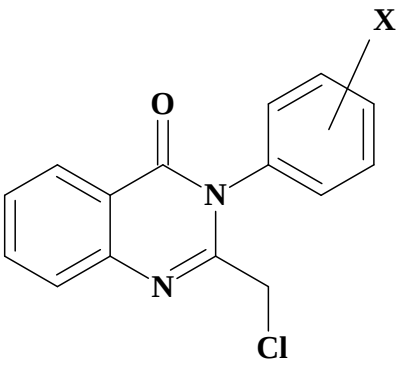


Deepak Gupta et al (2013) were reported **s**ynthesized a novel analogs of 2-phenyl-3-(3-(substituted-benzylideneamino)-quinazolin-4(3H)-one derivatives. Synthesized compounds screened for anticonvulsant activity. The outcome showed that 2-phenyl-3-(3-(propoxybenzylideneamino)-3H-quinazolin- 4-one is the main potential compound with the less side effects.[39]



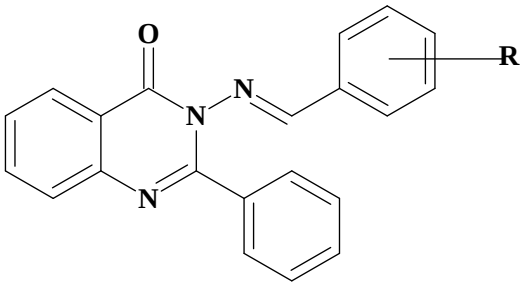
Meena K Yadav et al (2017) were reported synthesized a novel sequence of 4(3H)-quinazolinone N-1 (substituted- N-4[(4-oxo- 3-phenyl- 3, 4-dihydro-quinazoline- 2-ylmethyl) semi carbazones. Their anticonvulsant activity was evaluated by strychnine, thio- semicarbazide and 4-aminopyridine provoked

seizure models. Synthesized a novel sequence showed fine anticonvulsant activity.[40]

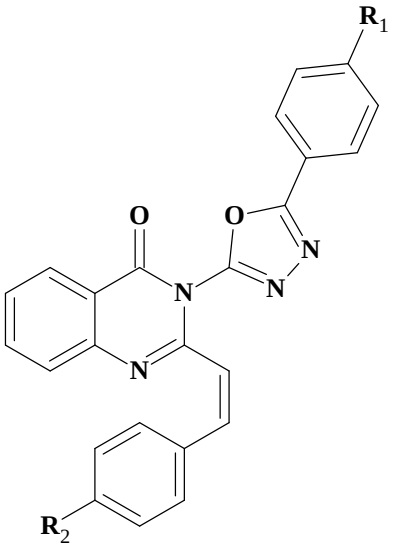


3.3 ANTIMICROBIAL ACTIVITY

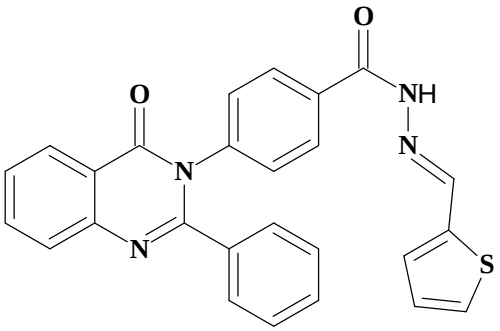
Ashis Kumar Nanda et al., (2007) were reported 3-(arylideneamino)-2-phenylquinazoline- 4(3*H*)-ones. It was revealed that incorporation of the 3-arylideneamino substituent enhanced the anti-bacterial activity of quinazolines ring.[41]



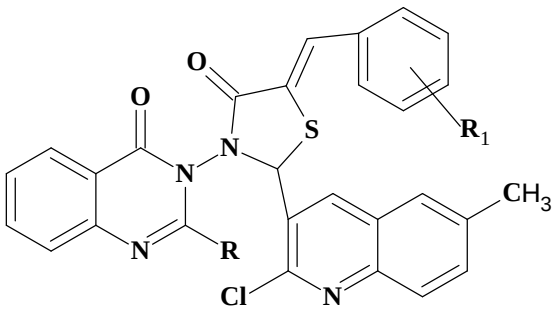
Vivek Gupta et al., (2008) were reported prepared many 3-[5-(4-substituted) phenyl-1, 3, 4-oxadiazole-2- yl]-2-styryl quinazoline- 4(3H)-one and they showed better antibacterial than antifungal activities in serial dilution technique.[42]



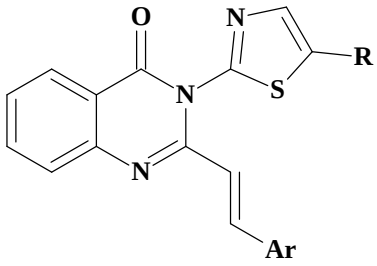
Mohamed T et al., (2010) were reported synthesized 5-Amino-4-cyano-1H-pyrazole derivatives. The synthesized derivatives showed moderate to high inhibition actions. Derivatives add in with a sugar moiety and a pyrazolyl ring in their structure showed the maximum antimicrobial activity.[43]



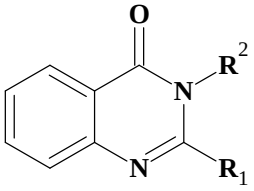
N.C. Desai and Amit M. Dodiya et al., (2011) were reported prepared a series of 2-(2-chloro-6-methyl (3-quinolyl))-3-[2-(4-chlorophenyl)-4-oxo(3-hydroquinazolin-3-yl)]-5-[(aryl)methylene]- 1,3-thiazolidin-4-ones. A few compounds with chloro or hydroxy group showed good quality antimicrobial action.[44]



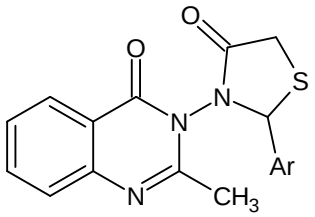
Chandresh L. Jagani et al., (2012) were reported prepared microwave assisted novel 3-thiazole substituted 2-styryl 4(3*H*)-quinazolinone analogues. The antibacterial actions of the synthesized analogues exhibited equivalent inhibitory effects compared to standards.[45]



Akhil A. Nagar et al., (2013) were reported 2, 3-di-substituted quinazolin-4-(3*H*)-ones and its analogues had synthesized at microwave irradiation and they showed moderate antimicrobial activity.[46]



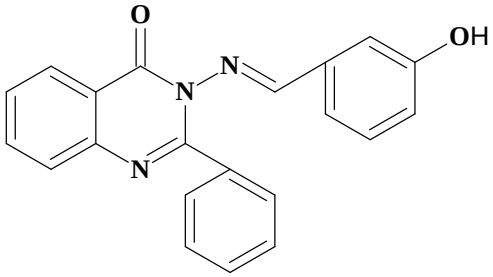
Shivanand et al., (2021) were reported Synthesis, Characterization of 2-methylquinozolinyl thiazolidines for antimicrobial activity. It was revealed that most of these quinazoline nucleus coupled with thiazolidinone could yield effective biologically active derivatives displayed 3-(4-oxo-2-arylthiazolidin-3-yl)-2-methylquinazolin-4(3*H*)-one derivatives moderate to good antimicrobial activity.[47]



Ar- Benzaldehyde or 2-chloroquinolin-3-carbaldehyde

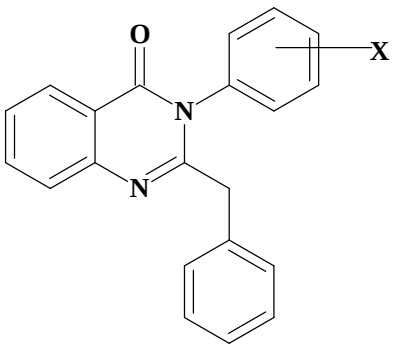
3.4 ANTI-HIV ACTIVITY

Krishnan Suresh Kumar et al., (2010) were reported synthesized a sequence of 3-(benzylideneamino)-2-phenylquinazoline-4(3*H*)-ones. Most of these derivatives displayed superior antiviralaction.[48]



3.5 ANTI-FUNGAL ACTIVITY

Anshu Dandia et al., (2004) were reported a series of fluorinated 2, 3-disubstituted quinazolin- 4(3*H*)-ones. Reported derivatives revealed average antifungal activity.[49]



4. CONCLUSIONS

In summary, Given the advances in methodology synthetic technology in recent years and the continued interest in the quinazoline backbone in medicinal chemistry and drug development, the development of Efficient and reliable methods for the construction of these molecules will ensure make this an active and important area of research in heterocyclic chemistry. The presence of a substituent at different positions of the quinazoline or quinazolinone moiety determines the biological activity. Inventions of new methods for their synthesis broaden their biological profile.

The results of the analgesic and anti-inflammatory activity indicate that the replacement of the C2 phenyl group of the phenyl3-2. substituted quinazolines with the C2 methyl group showed increased activity. However, the potency is lower than our previously reported 2,3-disubstituted quinazolines. Therefore, further structural modifications are planned in order to increase not only the analgesic and anti-inflammatory effect but also the antibacterial effect.

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CONFLICT OF INETEREST

The authors declare no conflict of interest.

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