Section: Research Paper

ROLE OF QUINAZOLINE IN BIOLOGICAL ACTIVITY: A REVIEW

Manoj Kumar[1], Sumit Kumar[2*],Dinesh Kumar[3], Suresh Kumar[4] and Deepti Sharma[5]

1. Department of Pharmaceutical Sciences, Guru Jambheshwar University of Science and Technology, Hisar-125001, Haryana, India

2*.Corresponding Author

Department of Pharmaceutical Sciences, Central University of Haryana, Jant-Pali, Mahendergarh 123031, India

Email-drsumitkumar@cuh.ac.in

3. Atam Institute of Pharmacy, Om Sterling global University, Hisar-125001, Haryana, India

4. Laureate Institute of Pharmacy, VPO-Kathog, Kangra, Himachal Pradesh-177101

5. Department of Pharmaceutical Sciences, Guru Jambheshwar University of Science and Technology, Hisar-125001, Haryana, India

ABSTRACT

Due to its diverse applicability in the realm of medicine, the heterocyclic fused nucleus quinazoline has attracted a lot of attention in recent years research in chemistry. A number of patents and studies on the discovery and development of novel potential quinazoline compounds have been published in the literature. Quinazoline and their derivatives are a type of chemical substance that is very prevalent.

Chemicals that are the most active and have a wide variety of biological effects actions such as antibacterial, antifungal, and antiviral properties antifungal, anti-HIV, analgesic, antimicrobial, anti-inflammatory, anticancer, and antihypertensive antioxidant, analgesic, anticonvulsant, anti-malarial, anticancer, and anti-tubercular properties.

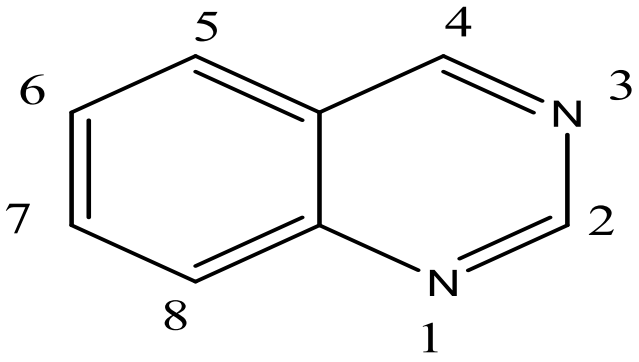
The goal of this review was to compile research on Quinazoline for its diverse pharmacological effects described by researcher's activities, as well as recent attempts on this subject.

Key words: Quinazoline, Antimalarial,Anti-diabetic, Anti-inflammatory, Anticonvulsant activity.

INTRODUCTION

Heterocyclic compounds are exhibited a very important role in medicinal sciences[1]Quinazoline and quinazolinones are also a part of heterocyclic compound family which is N-containing heterocyclic compound and its chemical formula is C8H6N2[2]Quinazoline and its derivatives are now a days in focus because of their various properties anti-cancer, anti-hypertensive, anti-microbial, antiinflammatory, antibacterial, anti-epileptic etc[3]

Quinazoline has benzene ring and the pyrimidine ring are two fused six-membered aromatic rings.[4]



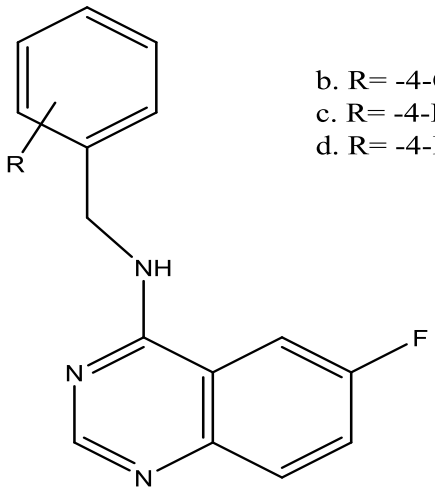
quinazoline

C8H6N2 ,Molarmass: 130.15 g mol−1

The aim of this review article to highlight the variousproperties of quinazoline and their derivatives reported by various reserchers on quinazoline and their derivatives.Quinazoline and its derivatives has a notable pharmacophore comes out as adaptable for various inhibition of various receptors and metabolic enzymes.[5]

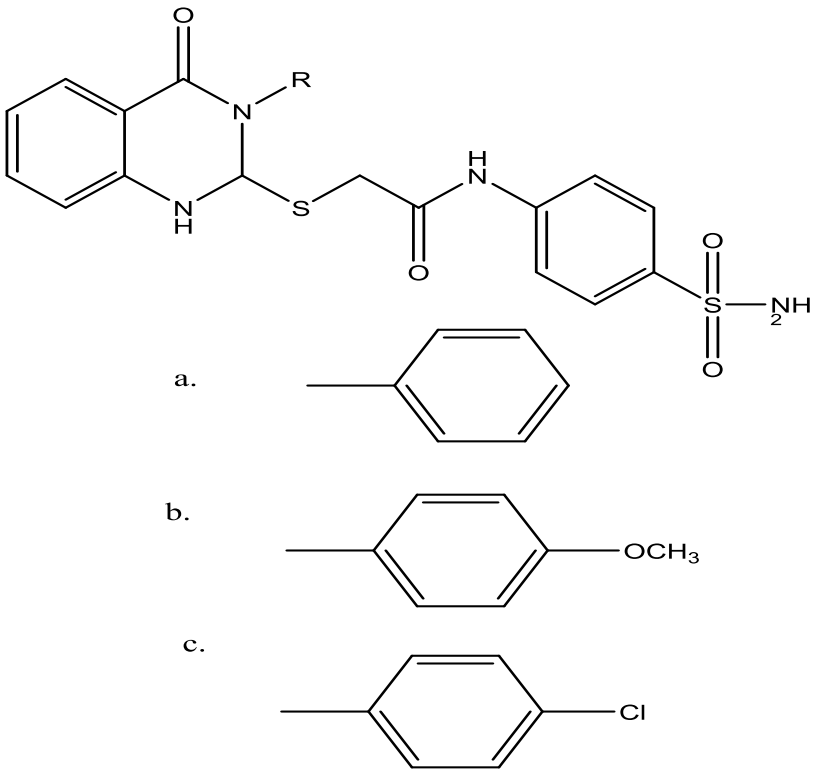
***Quinazoline as anticonvulsant agents:-**

F.zayed *et al* with their co team workers are synthesis derivative of N-substituted 6-fluoro-quinazolin-4-amine and their anti-convulsant properties are tested Subcutaneous pentylenetetrazole (ScPTZ) and maximum electroshock (MES) tests were used. [6]
In theitr study three compounds were showed potent anticonvulsant property 5b ,5c ,5d



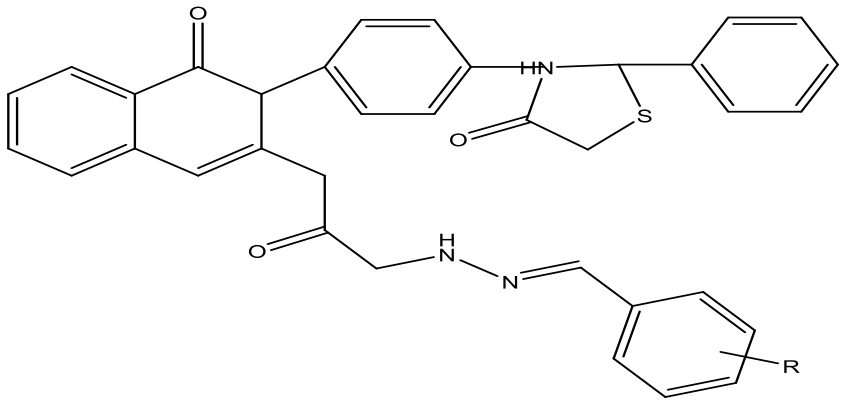
b. R= -4-Cl
c. R= -4-Br
d. R= -4-I

Sepheri *et al* with their co team workers synthesis quinazoline sulfonamide derivatives and evaluate their in-vitro properties antidiabetic anticholinergic anticonvulsant activity. This derivatives are found to be effective against various enzymes alpha-glycosidase, human carbonic anhydrase I and II ,butyrlcholinestrase and aectylcholinestrase enzymes[5]
In their invitro studythey found three potend molecules as below



Saravanan *et al* with their co team workers synthesis and evaluated 2(2-substituted benzylidenelyhydrazinyl2-oxopropyl-3-(4-[4-oxo-2-phenylthiazolodin-3-yl]penyl)quinazoline-4(3H) one MES and the subcutaneous pentylenetetrazole (ScPTz) test were used to evaluate their antiepileptic activity. Their biological activities of tested compound with chemical stuctures that electron donating compounds are higher activity then electron withdrawing groups.[7]

In their study compound 7c, 7g, 7h ,7i, 7l are more potend when compared with other compound found in which 7j with broad spectrum activity.



7c. 4- NO2, 7i. 4-NH2 , 7g. 4-CH3, 7h. 4-OH, 7l 3-OH

S.jangam *et al* with their co team workers synthesis quinazoline and thiazoline moiety 3(2-substituted-4-oxothiazolidine-3-yl)-2-phenylquinazolin-4(3H)one and evaluate their anti-convulsant activity in vivo by using maximal electro shock and induce convulsio at a dose of

25mg/kg.

In their study compound 3d were found more potend and show noteworth*y* anticonvulsant activity.

Han *et al* in their study demonstrated that diverse modes of action, such as chlorination, chloramination, and ozonation, cause differences in cytotoxicity and genotoxicity of carbamazepine an antiepileptic drug they investigated that ozonation increase the genotoxicity and highest cytotoxicity.[8]

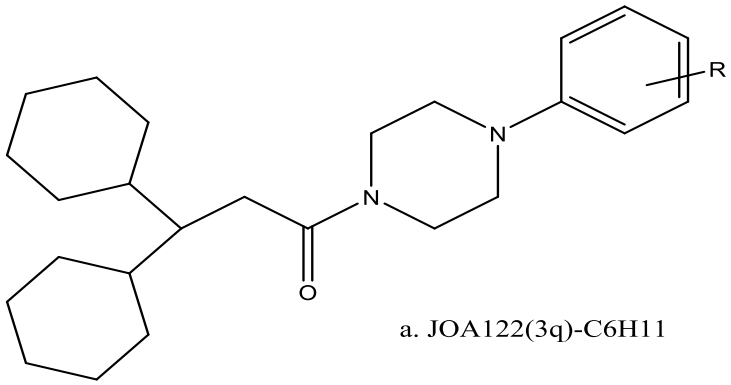
They evaluated and compare dissimilarities in genotoxicity during chlorination chloramination and ozonation disinfection.[8]

Chromosomal or DNA damage on CHOKI cells was found by CBZ and it cause cytotoxicity[8]

2 isomers (10)H-acridone and TP-237 are produce during chlorination and chloramination are found TP and CBZ and they are forecast to be DNA damaging agents.[8]

Rapaz *et al* with their co team workers are synthesis derivatives of epiletic molecule 3,3-dipenyl-propionamides in their previous work they also found some non epileptic activity like analgesic in their recent resreach on same molecule and their aim to show the nonepileptic characters in this study[9]

In their study they found compound JOA 122(3q) shows high affinity to voltage gated sodium channels and for 5HT receptor.[9]



a. JOA122(3q)-C6H11

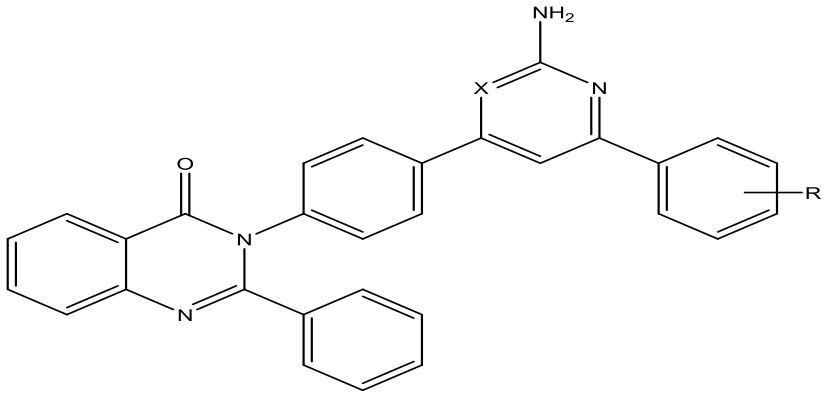
V.Natchinmuthu *et al*with their co team workers synthesis an intermediate by reacting pyrrole molecule and benzodiazepine with benzoic acid in DMF which can directly target voltage gated potassium channels and shows morepharmacological activity than currently available potassium channel blockers.[10]

They found the intermediate Molecular docking was used to determine the affinity A computer-aided algorithm predicted the ADMET and bioactivity of N-cyclohexyl-N-(cyclohexylcarbmoyl-4-(trifluoromethyl)benzamide for potassium protein structural characteristics. noticeable activity against potassium channel ions.[10]

Jain *et al* with their co team workers was synthesis 2-phenyl substituted derivative and MES seizures subcutaneous pentylenetetrazole was used to test their anticonvulsant activity. [11] To determine the binding mechanism of all produced compounds to Gamma- aminobutyricacid type A (GABAA) receptor, molecular docking was used in order to qualitatively justify their anticonvulsant actions.[11]

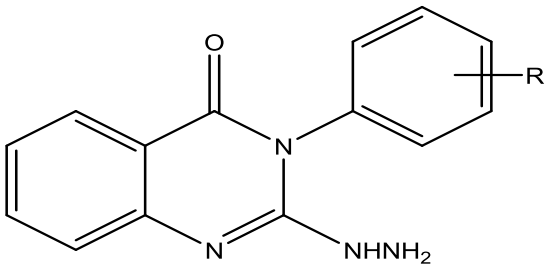
Anticonvulsant action was observed in all of the newly synthesised drugs. Two compounds, 5a and 5d, exhibited promising action, whereas the others exhibited modest

activity.[11]

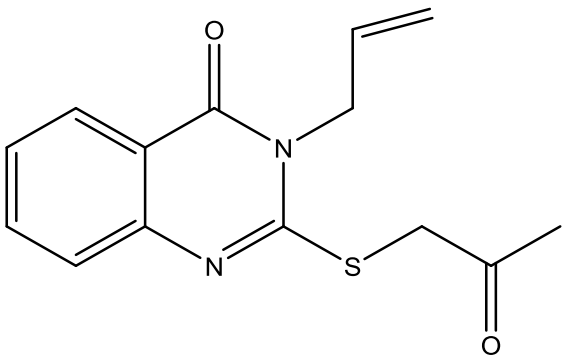


5a. X-O, R= 4-NO2
5d. X-S, R= 4-NO2

Zhang *et al* with their co team workers were synthesised qunazoline evaluate derivatives with triazole and other heterocyclic substituents
Neurotoxicity testing using maximum electroshock and rotarod
were used to assess the compounds' anticonvulsant efficacy and neurotoxicity.[12]
Among all compounds 6o and 6q demonstrated considerable oral efficacy against MES-induced seizures in mice.[12]



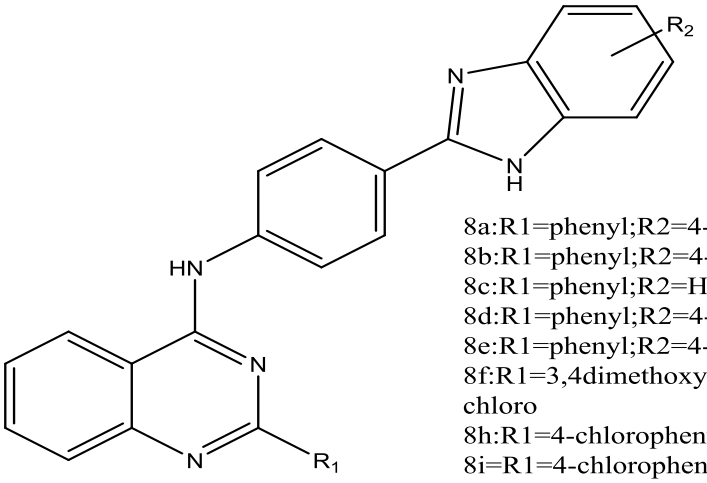
6o.p-Cl
6q.m-Br
Abulkhair *et al* with their co team workers demonstrate a series of quinazoline derivatives.
The anticonvulsant action of -quinazolinone derivatives against pentylenetetrazole was investigated and Maximal electroshock test and produced convulsions.[13]
In mice, the medicines methaqualone and sodium valproate were compared to the reference medicines. [13]



R1 = CH3 , 4-ClC6H4 , 4-BrC6H4 , 4-CH3C6H4 and 4-NO2C6H

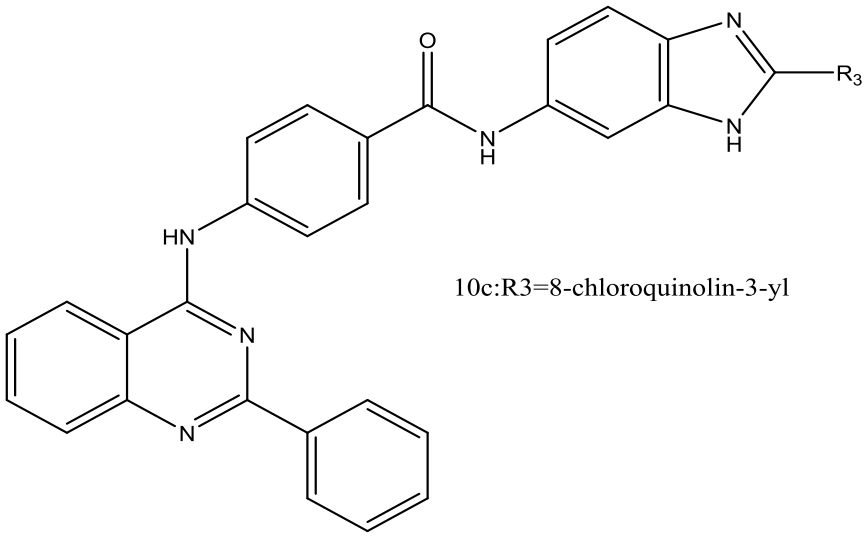
***Quinazoline as antimicrobial agents**:-

Malasala *etal*withtheir co team members demonstrate quinazoline 15 new molecules.
S. aureus and M. tuberculosi H37Rv were used to test their antibacterial activity.[14]
The anti-bacterial agents 8a, 8b, 8c, 8d, 8f, 8g, 8h, 8i, and 10c were discovered as a highest activity result of these experiments. These compounds were discovered to be less hazardous to Vero cells and shows positive selectivity index. [14]



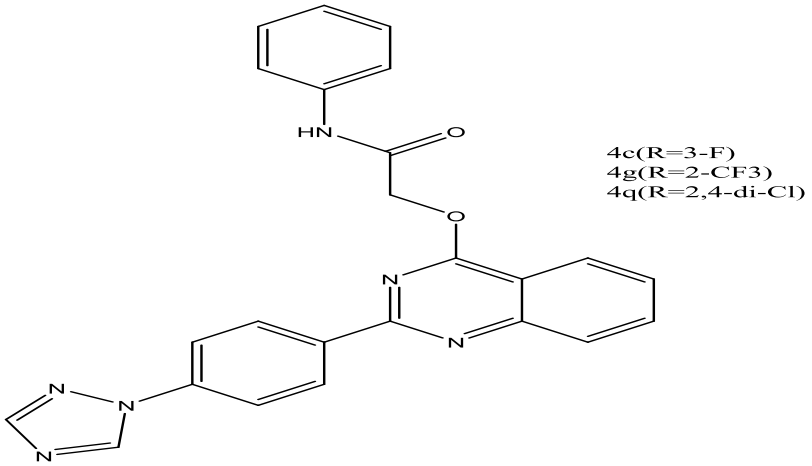
8a:R1=phenyl;R2=4-nitro
8b:R1=phenyl;R2=4-chloro
8c:R1=phenyl;R2=H
8d:R1=phenyl;R2=4-fluoro
8e:R1=phenyl;R2=4-bromo
8f:R1=3,4dimethoxyphenylphenyl;R2=4-chloro
8h:R1=4-chlorophenyl;R2=H
8i=R1=4-chlorophenyl;R2=4-fluoro

8a-j



10c:R3=8-chloroquinolin-3-yl

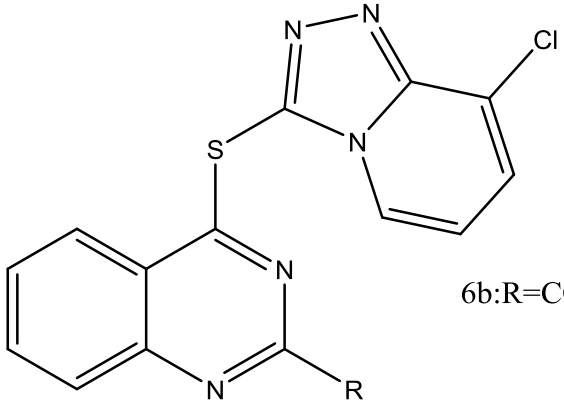
Fan *et al* with their co team members synthesis and evaluate derivative of quinazoline.
In agricultural settings, all of the compounds were examined in vitro for their potential to inhibit a number of important phytopathogenic bacteria and fungi. . The findings revealed that a number of substances had. significant antibacterial action against Xanthomonas oryzae pv. [15]
Compounds 4c, 4g, and 4q have strong activity against this bacterium, being 1.5 times more active than bismerthiazol, a commercial bactericide.



Fan *et al* with their co team members synthesis derivative of quinazoline molecule and evaluate their anti microbial activity in agriculture

Among these, the compound structure was further confirmed using a single-crystal x-ray diffraction analyser compound.[16]

In vitro antibacterial activity of some of the compounds against the phytopathogeni bacteria investigated is noteworthy, according to the bioassay results. The most active compound in the series, 6b, has the lowest molecular weight and the maximum hydrophilicity. [16]



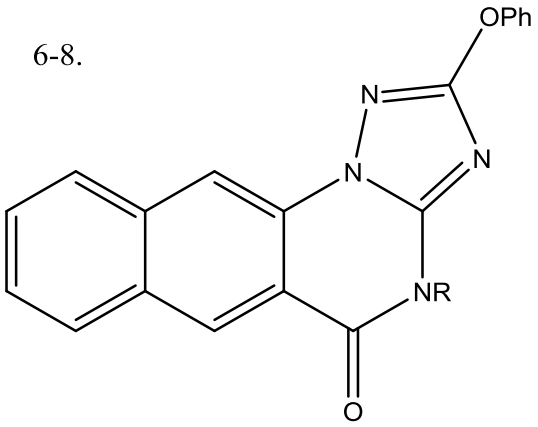
6b:R=CO2C2H5

Abuelizz *et al*with their co team members synthesis and evaluate quinazoline molecule and identified them by physiochemical and spectra mean

The researchers tested them five Gram-negative and five Gram-positive clinically pathogenic bacterial strains were tested in vitro as well as 10 fungus strains.[17]

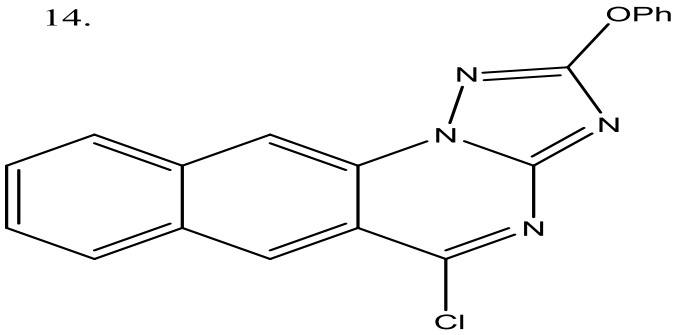
Antibacterial reference drugs was ampicillin and gentamicin. medications, while amphotericin B was employed as a control as the preferred antifungal drug the studied chemicals 6–8, 11, 12, and 14–16 had the strongest antibacterial activity against bacterial and fungal strains, according to antimicrobial investigations. .[17]

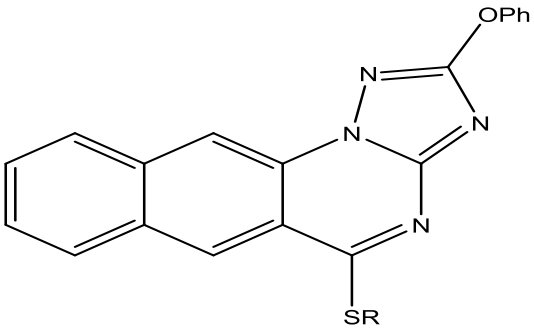
6-8.



6.R=3-CN-benzyl
7.R=4CN-benzyl
8.R=4Cl-benzyl
11.R=2-morpholinoethyl
12.R=2-(phtalimido-2-yl)propyl

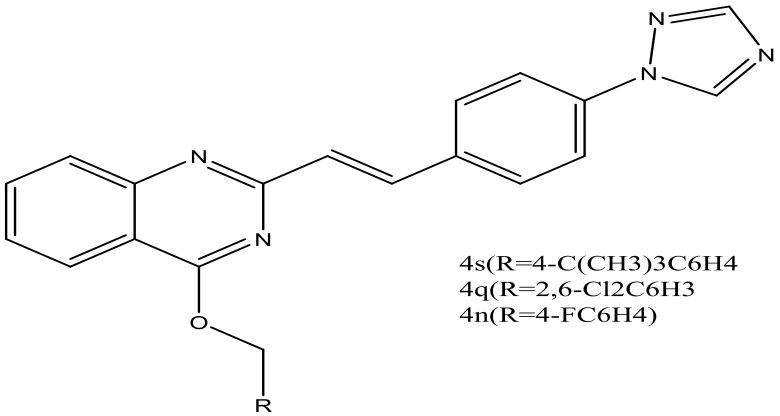
14.





16.R=S-allyl (17);

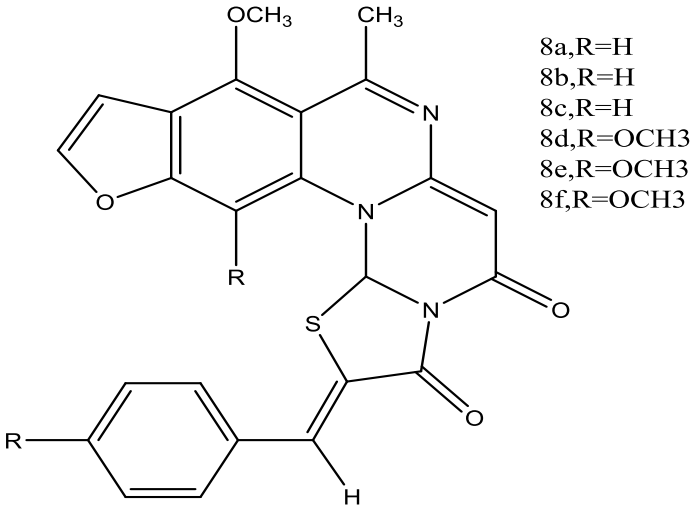
Yang *etal* with their co team members synthesis and evaluate derivative of quinazoline.1H NMR, 13C NMR, HRMS, and IR spectra were used to thoroughly characterise their structures. However, no one chemical has been shown to successfully block three harmful bacteria.[18]



4s(R=4-C(CH3)3C6H4
4q(R=2,6-Cl2C6H3
4n(R=4-FC6H4)

Hashem were synthesis substituted quinazoline derivative spectral data (IR, 1H-NMR, etc.) was used to deduce the structures of the produced compounds.

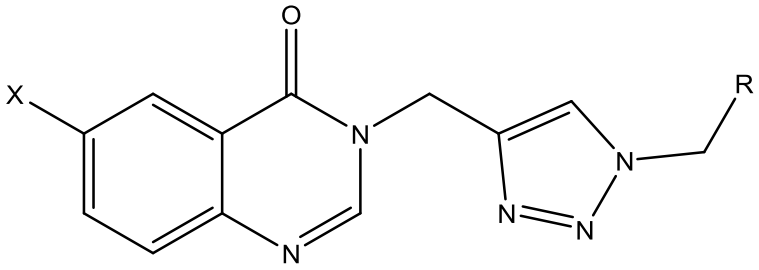
This research makes use of NMR, mass spectrometry, and elemental analysis. The antibacterial activity of the chemicals generated was evaluated against a variety of bacteria. Gram-positive, Gram-negative, and Gram-positive bacteria and fungi. [19]



8a,R=H
8b,R=H
8c,R=H
8d,R=OCH3
8e,R=OCH3
8f,R=OCH3

Glowocaka *et al* with their co team members synthesis derivative of quinazoline by the substitution of nitro and bromine on C6 position. Antibacterial activity was created and evaluated against Gram-positive and Gram-negative bacteria. [20]

Antifungal tests of compounds 9aa–aj, 9ba–bj, and 9ca–cj against Candida albicans ATCC 10231 and Aspergillus brasiliensis ATCC 16404. demonstrated notable activity of 9aa–aj.[20]



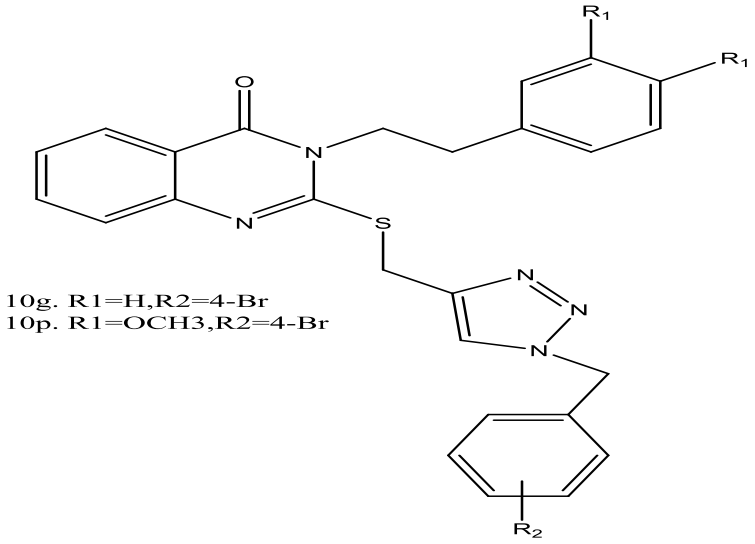
9aa-9aj
9ba-9bj
9ca-9cj

*Quinazoline as anti-diabetic agents:-

M.saeedi *etal* with their co team members was developed synthesised and assessed, leading to effective anti-diabetic medicines.

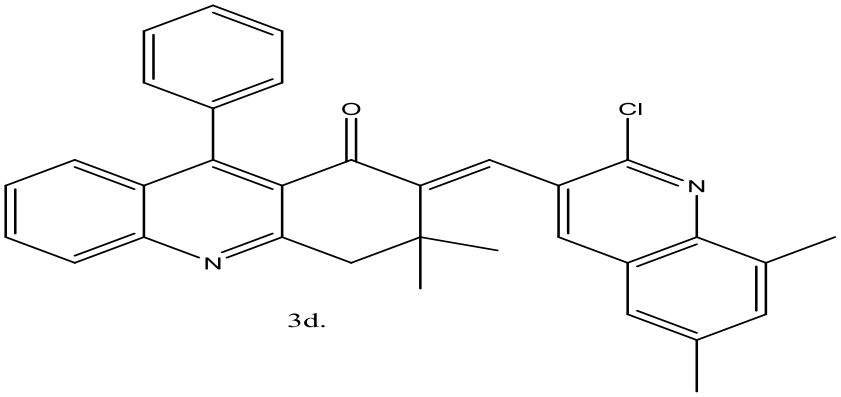
Even though all of the produced compounds had strong inhibitory action against yeast -glucosidase. The most effective were quinazolinone-1,2,3-triazoles with a 4-bromobenzyl moiety linked to the 1,2,3-triazole ring found more effective.[21]

The most active derivatives among the title compounds were discovered to be 10g and 10p.[21]

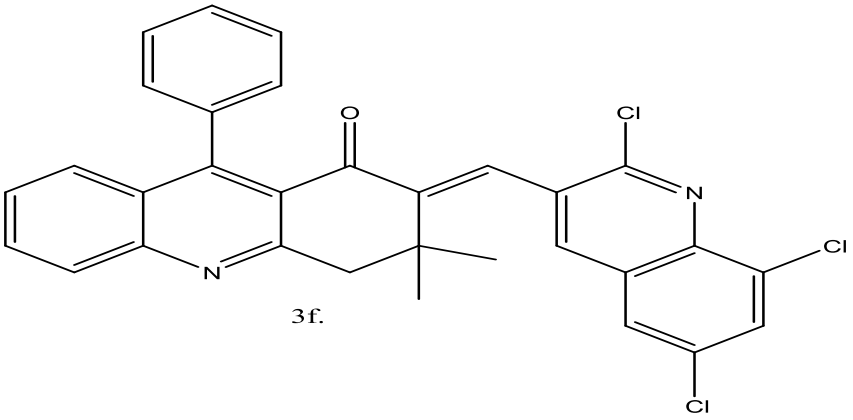


10g. R1=H,R2=4-Br
10p. R1=OCH3,R2=4-Br

Angajala *etal* with their co team members synthesis subsitituted series of quinazoline which are acridine analogoues these are derivative of carbaldehyde.
Reaction time is reduced, the work-up technique is straightforward, and the reaction is clean. Some of the notable aspects of the catalyst properties as it can be used up to 5 cycles.
The good hypoglycemic efficacy of compounds 3d and 3f is equivalent to those of standards pioglitazone and acarbose.



3d.

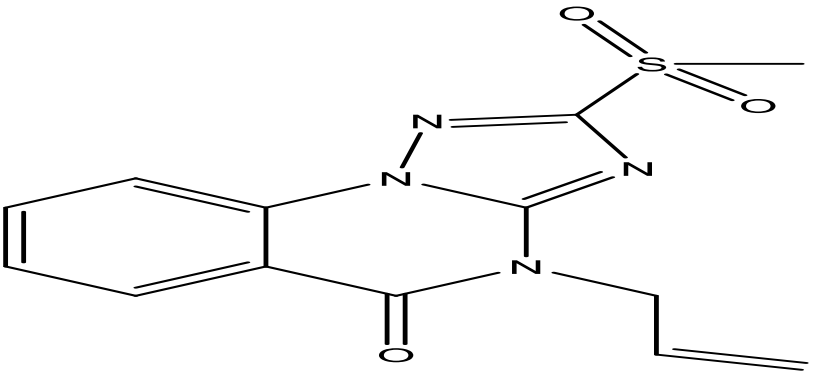


3f.

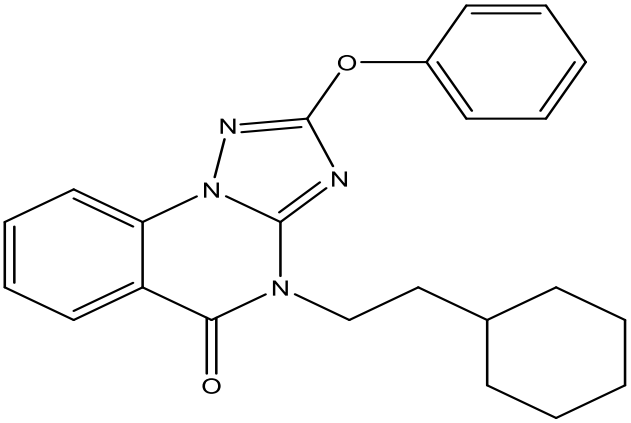
Abuelizz *etal* with their co team members synthesis and derive derivative of quinazoline molecules.The purpose of this investigation was to see how active the targets were in vitro as

-glucosidase inhibitors based on the Saccharomyces cerevisiae type -glucosidase enzyme.[22] Triazoloquinazolines 14, 8, 4, 5, and 3 were the most inhibiting activity studied in comparison to acarbose, which was used as a control.[22]

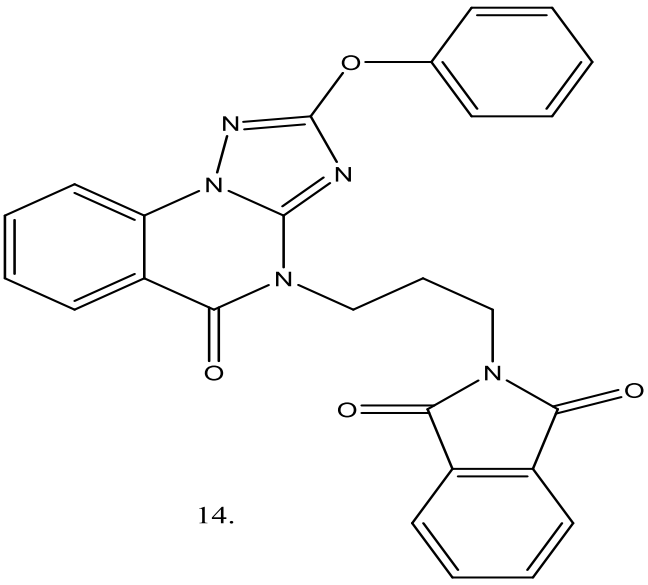
Triazoloquinazolines are a newly discovered class of potent -glucosidase inhibitors.[22]



8.



12.

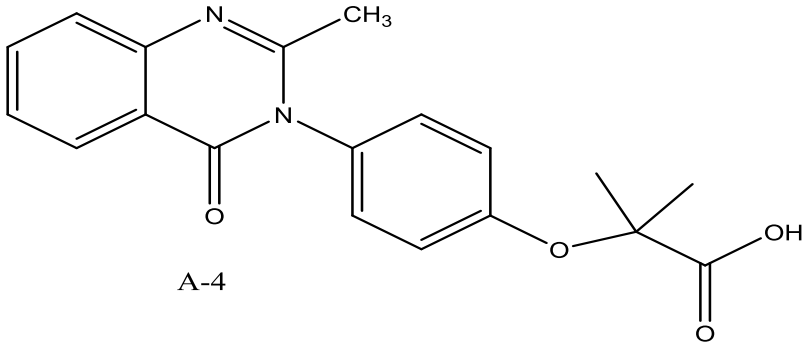


14.

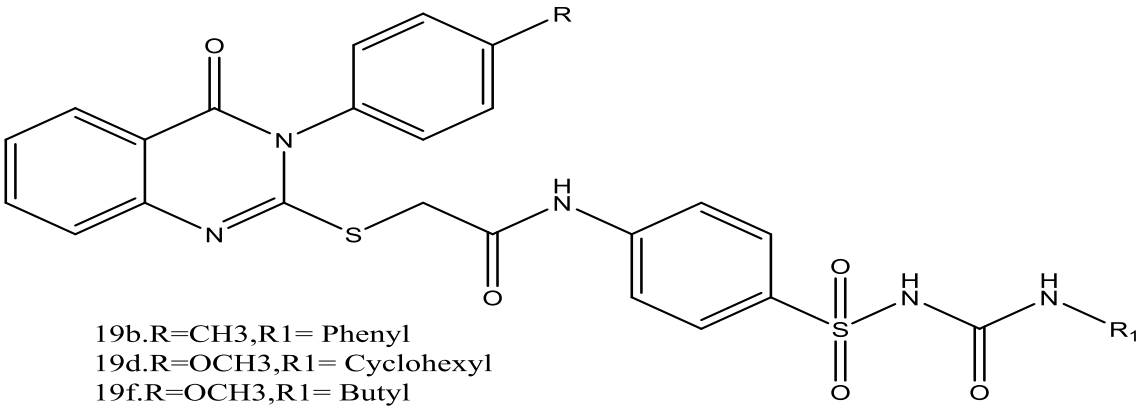
Mokale *et al* with their co team members synthesis derivative of quinazoline. A novel series

of substituted quinazoline derivatives was designed, synthesised, and tested in cholesterol-induced hyperlipidemic rats for their hypolipidemic activity.[23]

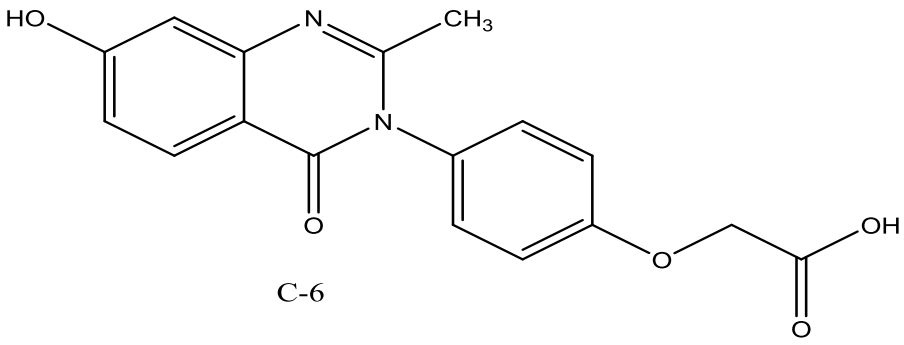
In vivo, compounds A-4, C-5, and C-6 were found to exhibit substantial antihyperlipidemic activity, lowering plasma levels of triglycerides (TG), While increasing levels of high-density lipoprotein (HDL), very low density lipoprotein (VLDL), and low density lipoprotein (LDL) (HDL). [23]



A-4



19b.R=CH3,R1= Phenyl
19d.R=OCH3,R1= Cyclohexyl
19f.R=OCH3,R1= Butyl

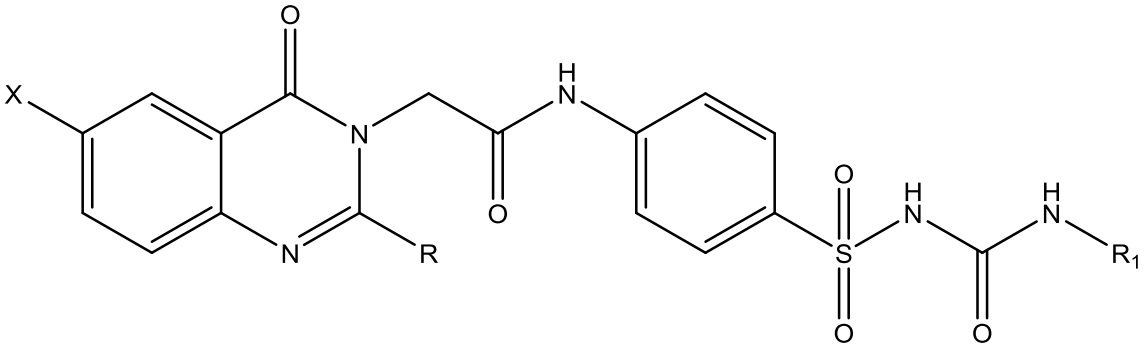


C-6

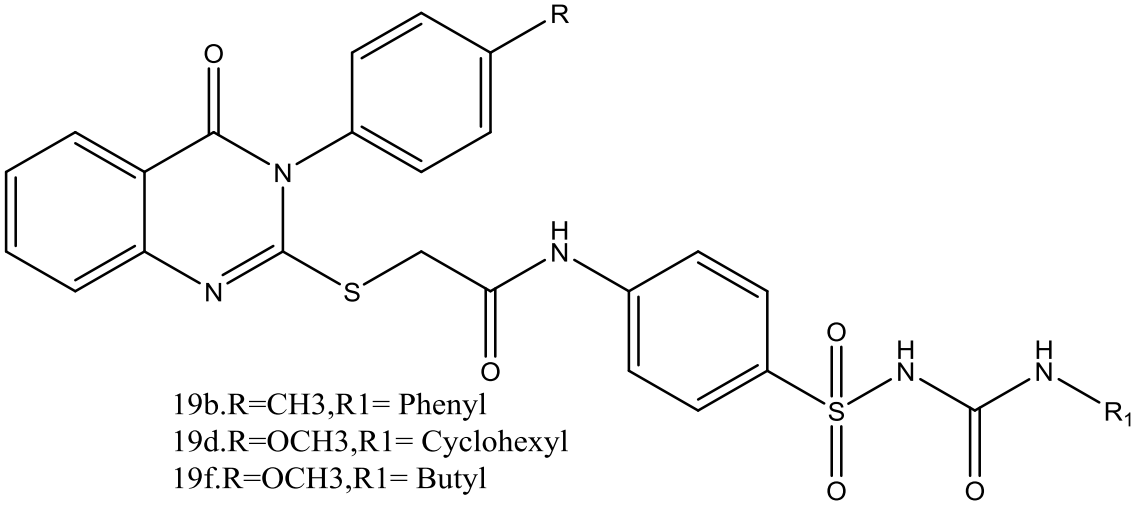
Ibrahim *et al* with their co team members synthesis derivative of quinazoline.The anti-hyperglycemic effects of the synthesised compounds were tested in vivo against hyperglycemic rats caused by STZ.

The PPARc binding affinities and insulin-secreting capacities of the 10 most active drugs were tested in vitro.[24]

The strongest affinities against PPARc were found in compounds 19b, 19d, 19f, 25f, and 25g, with IC50 values.



25f. X= Br, R =CH2CH3
25g. X =Br, R =CH3

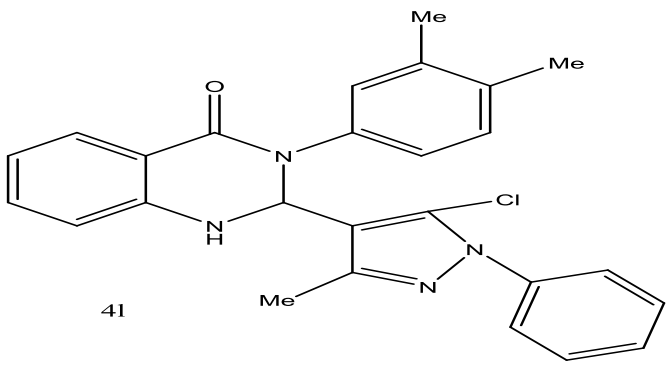


19b.R=CH3,R1= Phenyl
19d.R=OCH3,R1= Cyclohexyl
19f.R=OCH3,R1= Butyl

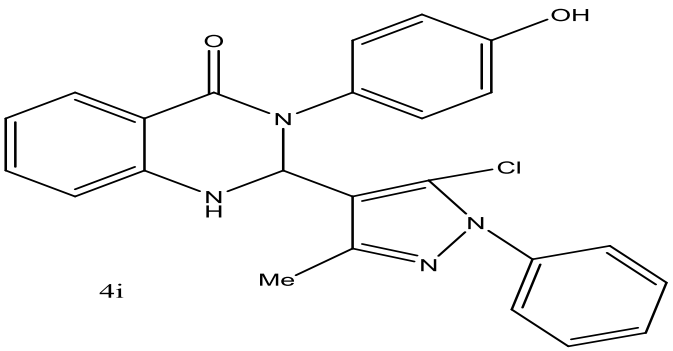
Barmak *et al*with their co team members synthesis quinazoline derivative aluminum is used In ethanol reflux, a catalyst is used to catalyse the condensation process between isatoic anhydride and aromatic aldehydes sulphate. .[25]

Their physical, IR, and structures were all confirmed H NMR, 13c NMR, and mass spectrometry data from spectroscopy was analysed for biological consequences.[25]

Molecules 4i and 4l, in particular, were a robust and amazing anti-glucosidase drug that bound to enzyme with considerable anti-glucosidase properties that matched the experimental data. .[25]



41

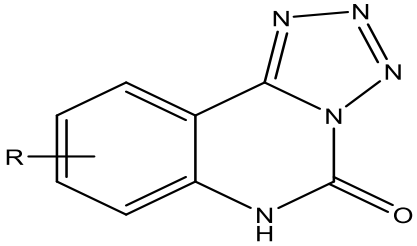


4i

Antypenko *et al* with co team members synthesis derivative quinazoline and their structures and purity of the compounds were assessed using IR, LC-MS, H-NMR, and elemental analytical dat

Depending on the reaction parameters, the products were separated and discussed. .[24]

Tetrazolo[1,5-c] quinazoline-5(6H)-one . 3.1 was found to be one of the most active compounds [24]



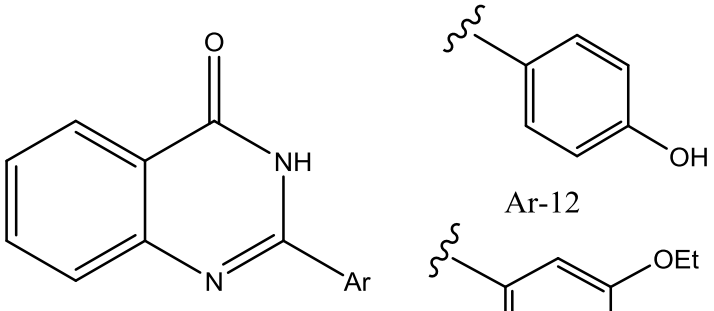
3.1 -H,

Javaid *et al* with their co team members synthesis 25 derivative of quinazoline were tested for a-glucosidase inhibitory activity in yeast (Saccharomyces cerevisiae).[26]

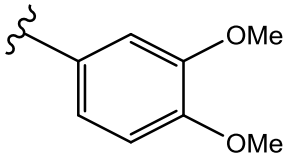
The routes of action of the most active compounds 12, 4, 19, and 13 were determined using enzyme kinetic studies.[26]

Molecular modelling approaches were also used to investigate the ways of inhibition of compounds 12, and 4.[26]

Ar -4.

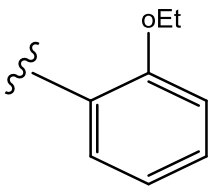


Ar -13

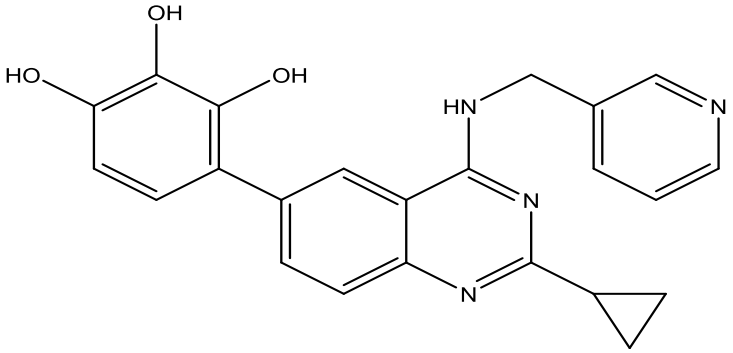


Ar-12

Ar-19.

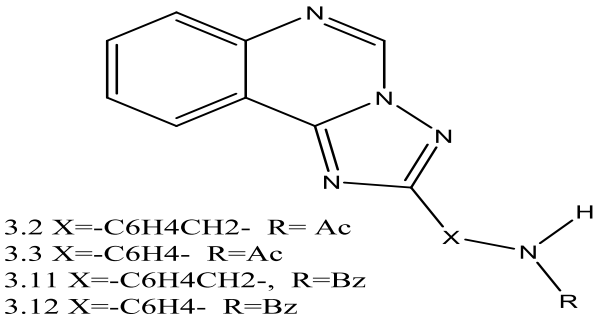


Gurram *et al* with their co team members synthesis derivative of twenty one quinazolineThe compounds' binding mechanism to the Glide docking approach was employed to examine the active site of a-glucosidase. [27]
Amidated at the C-4 position to produce a total of 21 compounds.
All of these compounds were chosen based on their interaction profile and docking score for enzymatic
screening in vitro
The compound 6f had the most inhibitory effect.[27]



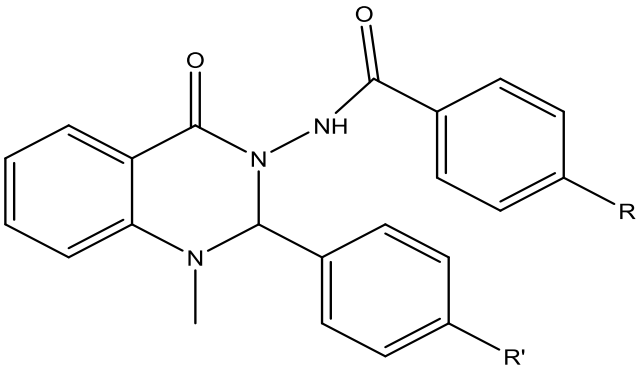
*<u>Quinazoline as anti-inflammatory:</u>-

Martynenko *et al* with their co team members synthesis derivative of quinazoline. Hydrazides are important intermediates in current organic chemistry because they are frequently utilised to make substituted alcohols [1,2,4]triazolo[1,5-c]quinazoline.[28]
The peculiarities of the synthesised compounds' structures were investigated using IR, NMR, and chromatography-mass spectrometry, which were subsequently analysed in detail. [28]



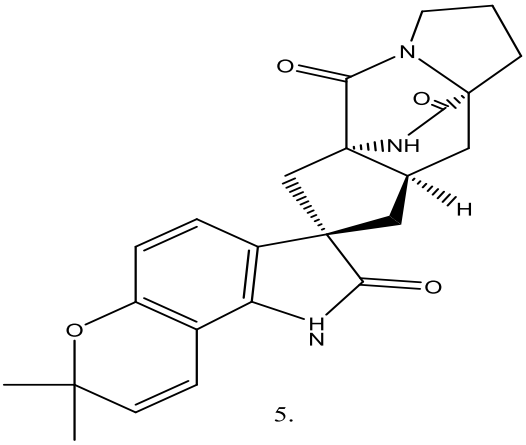
3.2 X=-C6H4CH2- R= Ac
3.3 X=-C6H4- R=Ac
3.11 X=-C6H4CH2-, R=Bz
3.12 X=-C6H4- R=Bz

Sakr *et al* with their co team members synthesis derivatives of quinazoline. The anti-inflammatory and analgesic medications, as well as COX-1/2 inhibitor, 1,4-dihydroquinazolin-3(2H)-yl benzamide derivatives (4a–o) have been devised and synthesised. .[29]
To confirm their chemical structures, 1H NMR, 13C NMR, and FTIR were employed. Elemental analysis and mass spectra.[29]
Compound 4b had the greatest overall results since it had a higher percentage of oedema inhibition (48%) than the reference medication diclofenac sodium (37.8%), as well as an analgesic effect is superior toboth indomethac and indomethacin.[29]

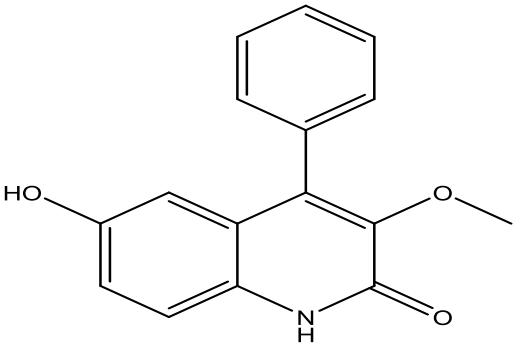


4b: R= 4-Cl R'= 4-Cl

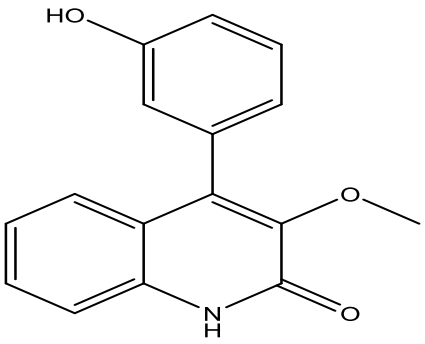
wang*et al* with their co team members synthesis derivative 2 new quinazoline. Aspergillus sp., a moss endophytic fungus, developed two novel quinazoline derivatives, versicomide E (1) and F. (2), as well as ten recognised compounds (3–12).
Their structures were determined by extensive spectroscopic data analysis and ECD computations.
NO production was significantly inhibited by compounds 5, 7, and 8.



5.



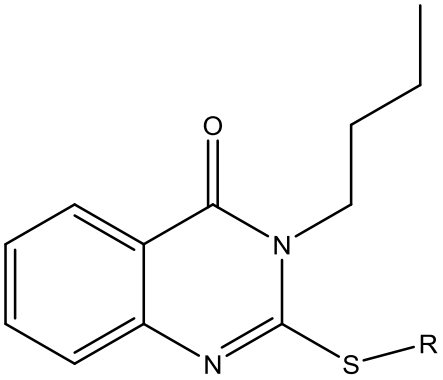
7.



8.

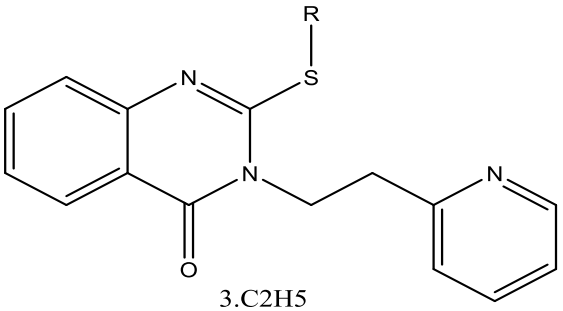
Abuelizz *et al* with their co team members synthesis derivative of quinazoline. The anti-inflammatory effect of 16 thioxoquinazolines was tested in vivo utilising a carrageenan-induced paw edoema experiment.[30]

The anti-inflammatory activity of compounds 4 and 6 was put to the testagainst full Freund adjuvantinduced arthritic rats and showed to be the most effective (80%).[30]
Compound 4 had nonselective activity against COX-1 and compound 6 had specific activity against COX-2.[30]



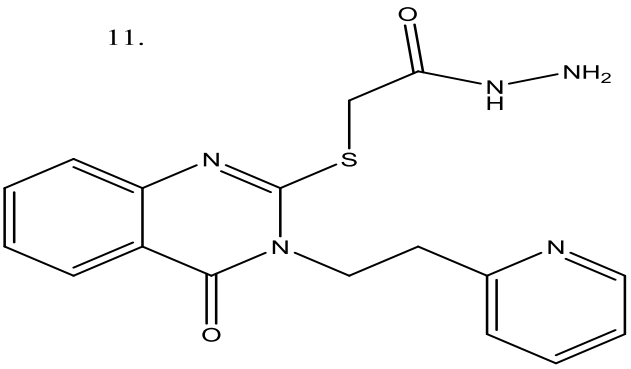
4. 2-Me-benzyl
6. 3-OMe-benzyl

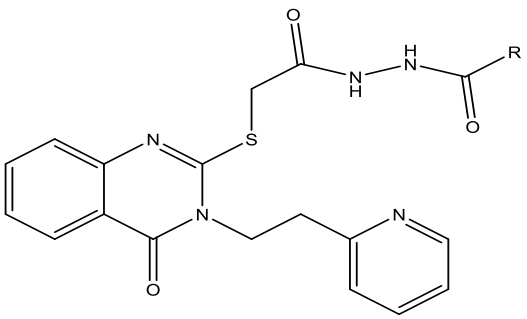
Abdel aziz *et al* with their co team members synthesis derivative of quinazoline tested for anti-inflammatory and analgesic properties in vivo, as well as cyclooxygenase inhibition in vitro COX-1/COX-2.[31]
With half-maximal effective doses, anti-inflammatory effects were seen in compounds 1, 3, 5, 11, 12, 13, 15, 17, and 25. [31]



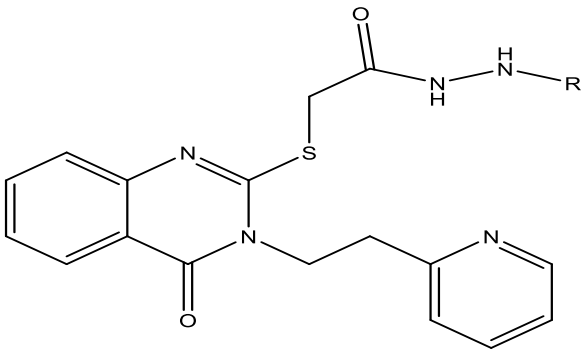
3.C2H5
5.4-Cl-CH2PH

11.

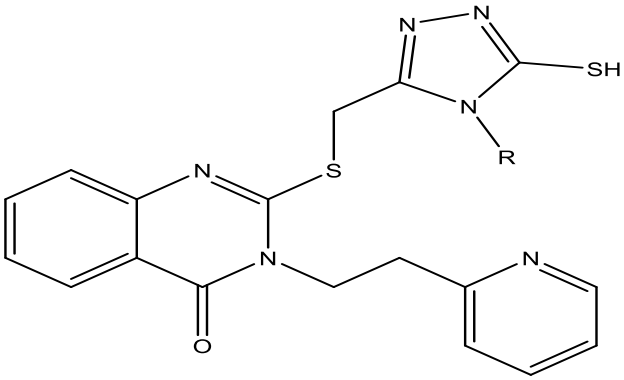




12. C2H5
13. Ph
15. 4-OCH3-Ph

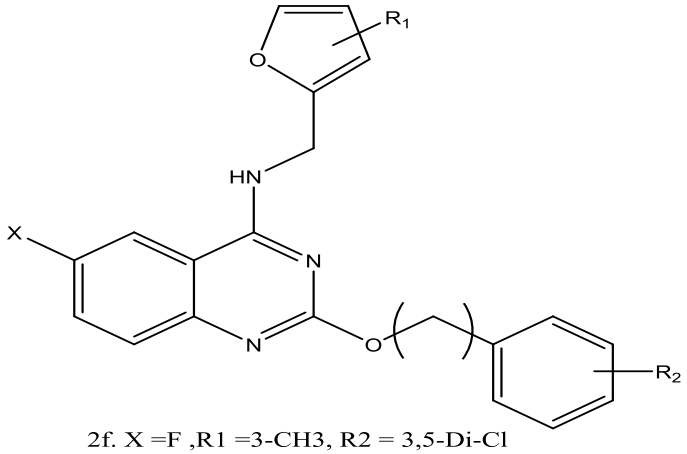


17. R = ET



25. R =Et

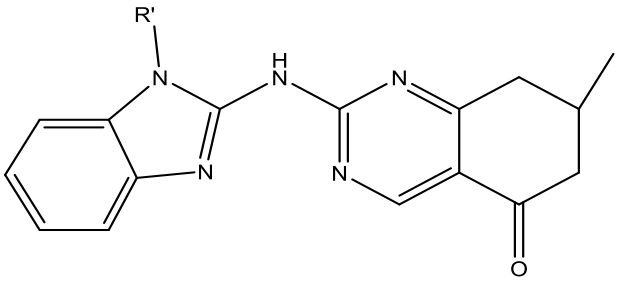
Cho *et al* with their co team members synthesis derivative of quinazoline they investigated the effects of a number of 2-aryloxy-4-amino-quinazoline derivatives as PAR2 antagonists in macrophages and investigate their influence on LPS-induced inflammatory responses .[32] With an IC50 value of 2.8 lM, compound 2f had the most antagonistic activity.[32]



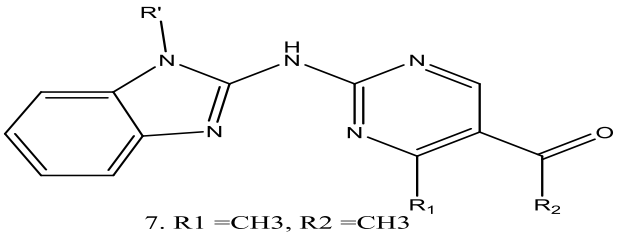
2f. X =F ,R1 =3-CH3, R2 = 3,5-Di-Cl

Prajapat with their co team members synthesis derivative of quinazoline. The anti-inflammatory properties of the resultant compounds were investigated in vivo efficacy against carrageenan-induced inflammation.

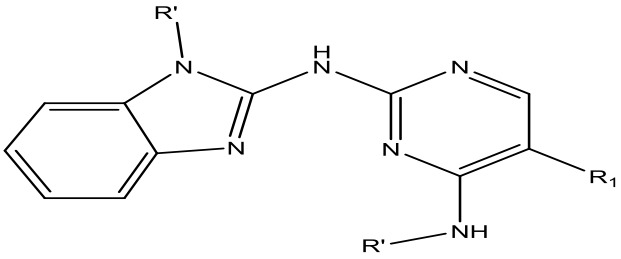
Anti-inflammatory drugs such as diclofenac were commonly utilised. When compared to typical drugs, some of the compounds showed significant anti-inflammatory effect.



6. C27H24N6O4



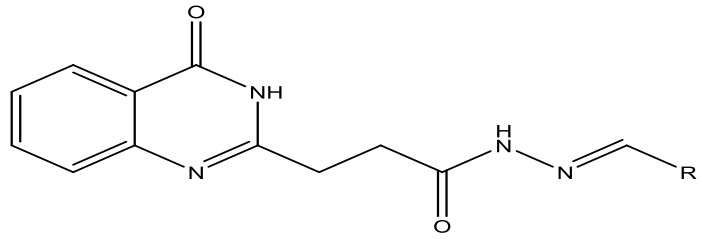
7. R1 =CH3, R2 =CH3



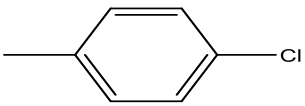
8a. R= COOH ,8b. R3= CN

Rakesh *et al* with their co team members synthesized derivative of quinazoline. A series of Schiff base derivatives generated from quinazolinone The antioxidants and anti-inflammatory substances 7–28 were produced and descry[33]

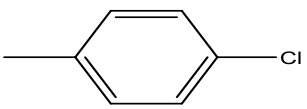
the anti-inflammatory activity of the produced compounds was tested in vitro, and the results showed that compounds 9–12 had outstanding anti-inflammatory activity.[33]



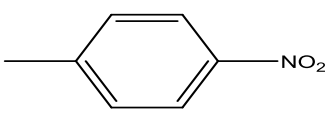
9.



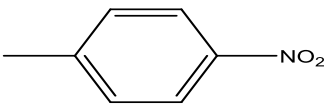
10.



11.

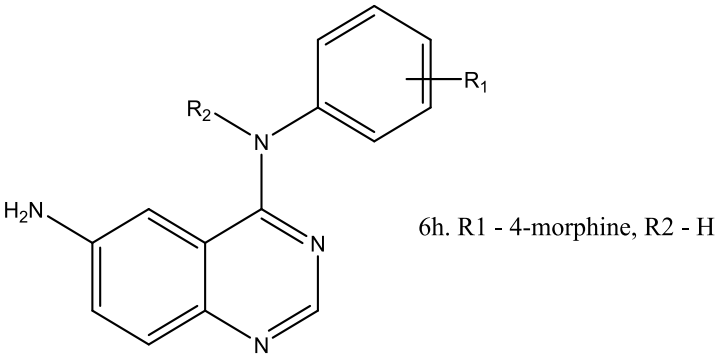


12.

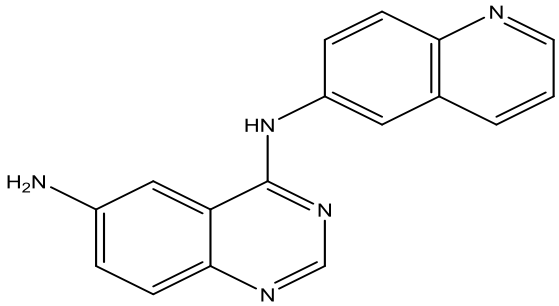


Hu *et al*with their co team members synthesized 33 derivative of quinazoline 4-amino quinazoline derivatives were produced and tested in a lipopolysaccharide-induced inflammatory model.[34]

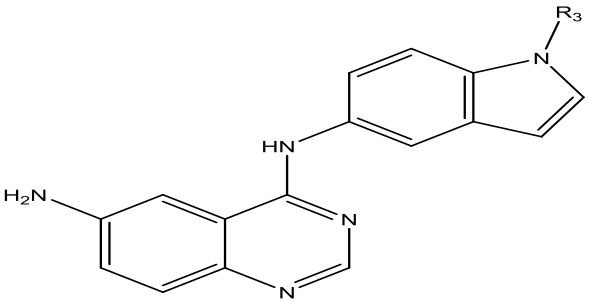
The goal of this work was to find novel quinazoline compounds with anti inflammatory properties that could prevent lipopolysaccharide-induced acute lung damage.[34]
6h, 6m, 6p, and 6q, the four most powerful drugs, showed dose-dependent inhibition TNF-alpha and Interleukin-6 production caused by lipopolysaccharide release.[34]



6h. R1 - 4-morphine, R2 - H



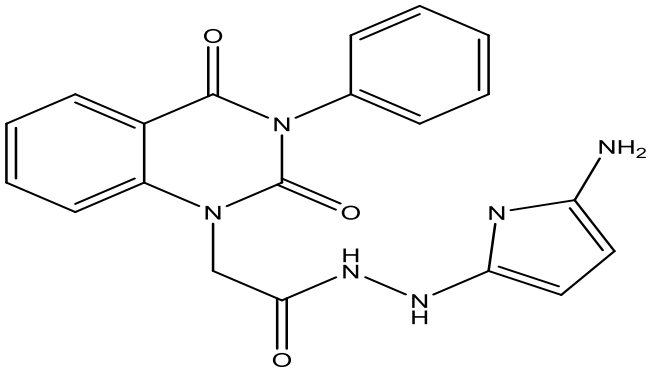
6m.



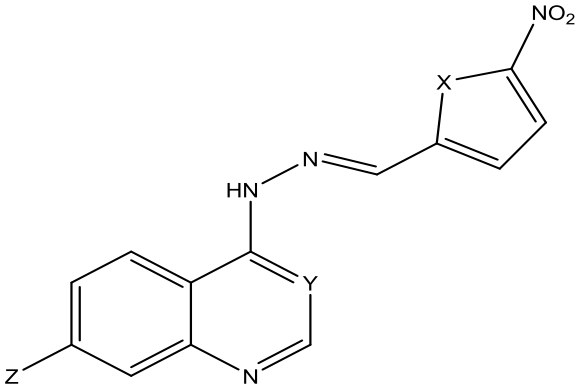
6p. R3= Methyl
6q. R3= propyl

*<u>Quinazoline as anti- malarial</u>

Abdelmonsef *et al* with their co team members synthesis derivative of quinazoline structure of the newly synthesised compounds was confirmed using 1H-NMR, 13C-NMR, MS, and elemental analysis.
In addition, an in silico molecular docking study of new compounds and a standard medicine (Chloroquine) was carried out for Investigate the different ways that Plasmodium falciparum (pfDHODH) interacts with its probable active site Dihydroorotate dehydrogenase.).
The antimalarial activity of freshly synthesised drugs is being determined utilising experimental approaches.
Compound 11 has the highest affinity for binding.

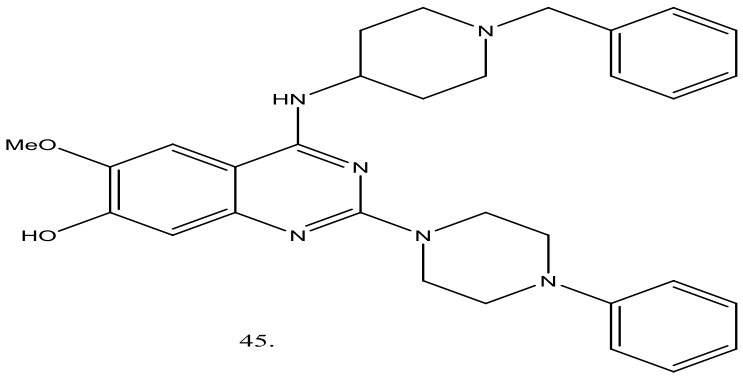


Tahghighi *et al* with their co team members synthesis derivative of quinazoline test synthesised drugs in vivo for molecular binding and antiplasmodial efficacy.
The binding of substances to haem and Plasmodium falciparum lactate dehydrogenase was studied using molecular docking (PfLDH).[35]
Antiplasmodial activity of the compounds were tested in mice using two conventional Peters' and Rane tests, which used chloroquine-sensitive Plasmodium berghei.[35]
Compound 3 was chosen for additional pharmacodynamic testing since it exhibited strong activity at the lowest dose.[35]

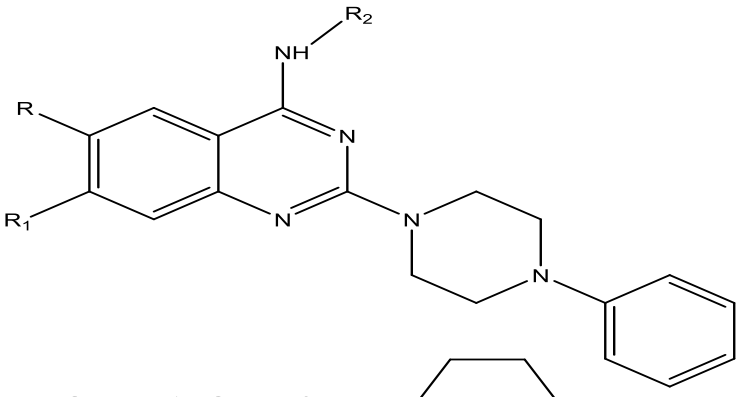


3. X= O; Y= N; Z= H

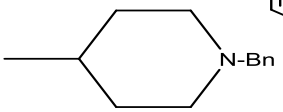
Bouchut *et al* with their co team members synthesis derivative of quinazoline. Plasmodium falciparum parasites were tested against a group of 51 compounds aimed at different epigenetic enzymes .[36]
The selectivity index criterion is based on in vitro activity against drug-resistant and drug-susceptible P. falciparum strains. four substances, one HDAC inhibitor (1), and three other compounds with excellent pharmacokinetic characteristics.[36]
These chemicals (37, 43, and 45) are good beginning points for developing new antimalarial drugs.[36]

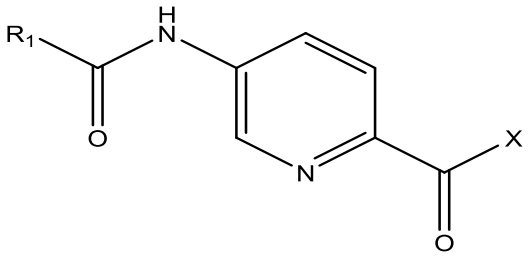


45.



43. R= OMe: R1= OBn: R2=



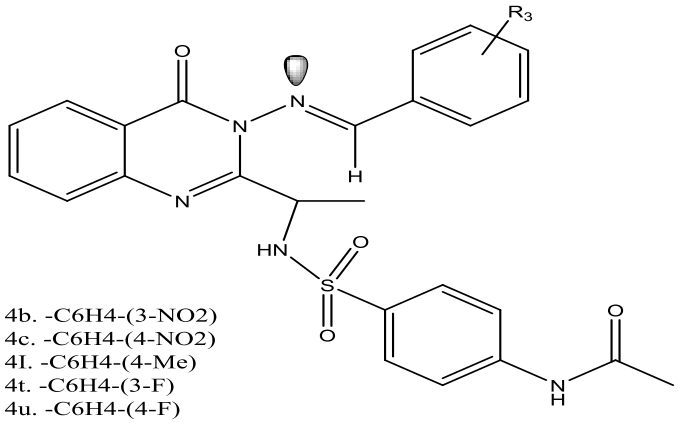


35. X= NHOH ; R1= 1-naphthylmethyl

Patel *et al* with their co team members synthesized derivative of quinazoline. The cyclization and integration of alanine linked sulphonamide in 4-quinazolin-(3H)-ones was achieved using Grimmel's approach, which was optimised and refined.

HPLC and spectroscopic measurements proved the purity and presence of a single isomer. The antimalarial potency of the produced sulphonamide connected 4-quinazolin-(3H)-ones hybrids was also tested, resulting in powerful entities (4b, 4c, 4 l, 4 t and 4u).

The hybrids that were active were gradually eliminatedand tested computationally and in vitro for enzyme inhibitory activity against the predicted receptors Pf-DHFR and h-DHFR, demonstrating their potency as dihydrofolate reductase inhibitors.



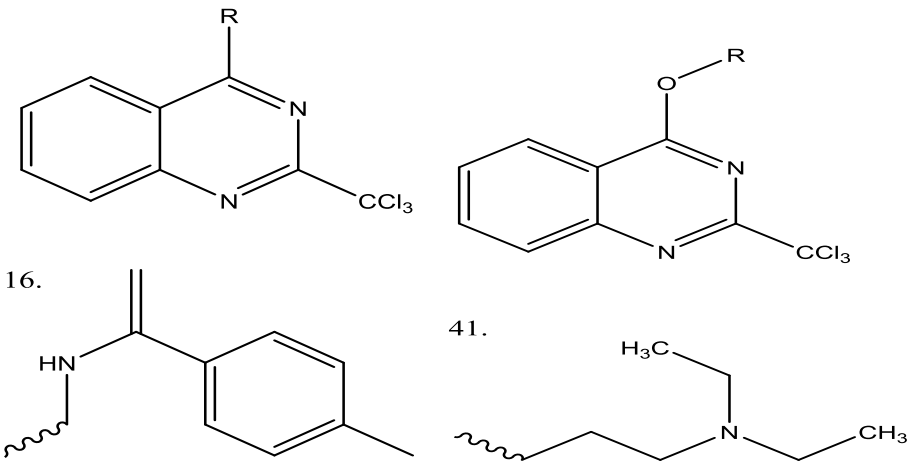
Amrane *et al* with their co team members synthesized derivative of quinazoline

By synthesising 42 new derivatives at position four of the quinazoline ring, we were able to undertake a structure-activity relationship (SAR) analysis.[37]

To find antiplasmodial compounds with likewise a carboxamido- or an alkoxy-group, to broaden our understanding of the antiplasmodial pharmacophore 2-trichloromethylquinazoline.[37]

There were five derivatives without a 2-CCl3 group. synthesised, tested, and found to be completely inert (EC50 > 50 M) for the two most powerful compounds (16 and 41).[37]

The antiplasmodial activity required the presence of a 2-trichloromethyl group.[37]



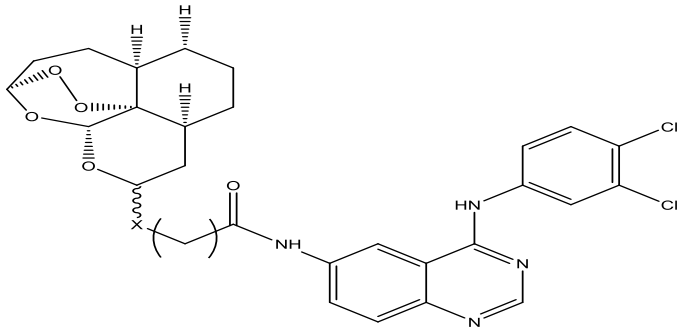
Frohlich *et al* with their co team members synthesized derivative of quinazoline

5 new quinazolineartemisinin hybrids were created and tested because of their biological action against malarial parasites in vitro Leukemia cells (CCRF-CEM and Plasmodium falciparum 3D7), Plasmodium falciparum 3D7, Plasmodium falciparum 3D7, Plasmodium falciparum 3D Human cytomegalovirus (CEM/ADR5000) and CEM/ADR5000.[38]

therapeutically utilised hybrid 9 (EC50 = 1.4 nM) are more afficient then DHA and chloroquin are two medicines that have been studied.

Inhibition of HCMV replication was particularly effective with chemicals 9 and 10 first-

generation cell cultures.



9. X =O(CO); n= 2
10. X = CH2; n= 0

CONCLUSION

Various structural elements are depicted in the compounds structure above.
quinazoline, and modifications around the fused ring after that, assess their efficacy in treating different types of diseases Using a variety of sources, I conducted a literature review.
Quinazoline derivatives have antibacterial, anti-inflammatory, and other properties like anticonvalsant, antimalarial, and other antifungal, antimalarial. They had a wide range of effects due to their varied physicochemical features.
As a result, we can infer that this review will undoubtedly benefit researchers. As a result, we can infer that this review will undoubtedly benefit researcher a significant impact in the treatment of a variety of deadly diseases.

REFRENCES

[1] D. Devipriya and S. M. Roopan, "UV-light intervened synthesis of imidazo fused quinazoline and its solvatochromism, antioxidant, antifungal and luminescence properties," *J. Photochem. Photobiol. B Biol.*, vol. 190, pp. 42–49, 2019, doi: 10.1016/j.jphotobiol.2018.11.003.

[2] M. Asif, "Chemical Characteristics, Synthetic Methods, and Biological Potential of Quinazoline and Quinazolinone Derivatives," *Int. J. Med. Chem.*, vol. 2014, pp. 1–27, 2014, doi: 10.1155/2014/395637.

[3] H. Xiao, P. Li, D. Hu, and B. A. Song, "Synthesis and anti-TMV activity of novel β-amino acid ester derivatives containing quinazoline and benzothiazole moieties," *Bioorganic Med. Chem. Lett.*, vol. 24, no. 15, pp. 3452–3454, 2014, doi: 10.1016/j.bmcl.2014.05.073.

[4] B. Kumar Tiwary, K. Pradhan, A. Kumar Nanda, and R. Chakraborty, "Implication of Quinazoline-4(3H)-ones in Medicinal Chemistry: A Brief Review," *J. Chem. Biol. Ther.*, vol. 01, no. 02, pp. 1–7, 2016, doi: 10.4172/2572-0406.1000104.

[5] N. Sepehri *et al.*, "Novel quinazolin–sulfonamid derivatives: synthesis, characterization, biological evaluation, and molecular docking studies," *J. Biomol. Struct. Dyn.*, vol. 0, no. 0, pp. 1–12, 2020, doi: 10.1080/07391102.2020.1847193.

[6] M. F. Zayed, S. K. Ihmaid, H. E. A. Ahmed, K. El-Adl, A. M. Asiri, and A. M. Omar, "Synthesis, modelling, and anticonvulsant studies of new quinazolines showing three highly active compounds with low toxicity and high affinity to the GABA-A receptor,"

Molecules, vol. 22, no. 2, pp. 1–15, 2017, doi: 10.3390/molecules22020188.

[7] G. Saravanan *et al.*, "Design, graph theoretical analysis, density functionality theories, Insilico modeling, synthesis, characterization and biological activities of novel thiazole fused quinazolinone derivatives," *Drug Dev. Res.*, vol. 79, no. 6, pp. 260–274, 2018, doi: 10.1002/ddr.21460.

[8] Y. Han *et al.*, "Chlorination, chloramination and ozonation of carbamazepine enhance cytotoxicity and genotoxicity: Multi-endpoint evaluation and identification of its genotoxic transformation products," *J. Hazard. Mater.*, vol. 342, pp. 679–688, 2018, doi: 10.1016/j.jhazmat.2017.08.076.

[9] A. Rapacz *et al.*, "Antiallodynic and antihyperalgesic activity of new 3,3-diphenyl-propionamides with anticonvulsant activity in models of pain in mice," *Eur. J. Pharmacol.*, vol. 821, pp. 39–48, 2018, doi: 10.1016/j.ejphar.2017.12.036.

[10] V. Natchimuthu, S. Bandaru, A. Nayarisseri, and S. Ravi, "Design, synthesis and computational evaluation of a novel intermediate salt of N-cyclohexyl-N-(cyclohexylcarbamoyl)-4-(trifluoromethyl) benzamide as potential potassium channel blocker in epileptic paroxysmal seizures," *Comput. Biol. Chem.*, vol. 64, pp. 64–73, Oct. 2016, doi: 10.1016/j.compbiolchem.2016.05.003.

[11] N. Jain, J. Jaiswal, A. Pathak, and P. K. Singour, "Central Nervous System Agents in Medicinal Chemistry Send Orders for Reprints to reprints@benthamscience.ae Central Nervous System Agents in Medicinal Chemistry Synthesis, Molecular Docking and Evaluation of 3-{4-[2-amino-4-(substitutedphenyl)-2H-[1, 3] oxazin/thiazin-6-yl} 2-phenyl-3H-quinazolin-4-one Derivatives for their Anticonvulsant Activity," vol. 18, pp. 63–73, 2018, doi: 10.2174/1871524917666170104142O.

[12] H. J. Zhang, P. Jin, S. Ben Wang, F. N. Li, L. P. Guan, and Z. S. Quan, "Synthesis and Anticonvulsant Activity Evaluation of 4-Phenyl-[1,2,4]triazolo[4,3-a]quinazolin-5(4H)-one and Its Derivatives," *Arch. Pharm. (Weinheim).*, vol. 348, no. 8, pp. 564–574, 2015, doi: 10.1002/ardp.201500115.

[13] H. S. Abulkhair, K. M. El Gamal, K. El Adl, and M. F Fadl, "Molecular Docking, Synthesis and Biological Evaluation of Some Novel 2-Substituted-3-allyl-4(3H)-quinazolinone Derivatives as Anticonvulsant Agents," *Med. Chem. (Los. Angeles).*, vol. 6, no. 9, pp. 593–603, 2016, doi: 10.4172/2161-0444.1000404.

[14] S. Malasala *et al.*, "Synthesis and evaluation of new quinazoline-benzimidazole hybrids as potent anti-microbial agents against multidrug resistant Staphylococcus aureus and Mycobacterium tuberculosis," *Eur. J. Med. Chem.*, vol. 212, p. 112996, 2021, doi: 10.1016/j.ejmech.2020.112996.

[15] Z. Fan, J. Shi, N. Luo, and X. Bao, "Synthesis, crystal structure and antimicrobial activity of 2-((2-(4-(1H-1,2,4-triazol-1-yl)phenyl)quinazolin-4-yl)oxy)-N-phenylacetamide derivatives against phytopathogens," *Mol. Divers.*, vol. 23, no. 3, pp. 615–624, 2019, doi: 10.1007/s11030-018-9896-2.

[16] Z. Fan, J. Shi, N. Luo, M. Ding, and X. Bao, "Synthesis, Crystal Structure, and Agricultural Antimicrobial Evaluation of Novel Quinazoline Thioether Derivatives Incorporating the 1,2,4-Triazolo[4,3- a]pyridine Moiety," *J. Agric. Food Chem.*, vol. 67, no. 42, pp. 11598–11606, 2019, doi: 10.1021/acs.jafc.9b04733.

[17] H. A. Abuelizz, R. A. El-Dib, M. Marzouk, and R. Al-Salahi, "In vitro evaluation of new 2-phenoxy-benzo[g][1,2,4]triazolo[1,5-a]quinazoline derivatives as antimicrobial agents," *Microb. Pathog.*, vol. 117, pp. 60–67, Apr. 2018, doi: 10.1016/j.micpath.2018.02.018.

[18] L. Yang, S. Ge, J. Huang, and X. Bao, "Synthesis of novel (E)-2-(4-(1H-1,2,4-triazol-1-yl)styryl)-4- (alkyl/arylmethyleneoxy)quinazoline derivatives as antimicrobial agents," *Mol. Divers.*, vol. 22, no. 1, pp. 71–82, 2018, doi: 10.1007/s11030-017-9792-1.

[19] A. A. Abu-Hashem, "Synthesis of new furothiazolo pyrimido quinazolinones from visnagenone or khellinone and antimicrobial activity," *Molecules*, vol. 23, no. 11, 2018, doi: 10.3390/molecules23112793.

[20] I. E. Głowacka, P. Grzonkowski, P. Lisiecki, Ł. Kalinowski, and D. G. Piotrowska, "Synthesis and antimicrobial activity of novel 1,2,3-triazole-conjugates of quinazolin-4-ones," *Arch. Pharm. (Weinheim).*, vol. 352, no. 3, pp. 1–14, 2019, doi: 10.1002/ardp.201800302.

[21] M. Saeedi *et al.*, "Design and synthesis of novel quinazolinone-1,2,3-triazole hybrids as new anti-diabetic agents: In vitro α-glucosidase inhibition, kinetic, and docking study," *Bioorg. Chem.*, vol. 83, pp. 161–169, Mar. 2019, doi: 10.1016/j.bioorg.2018.10.023.

[22] H. A. Abuelizz, E. H. Anouar, R. Ahmad, N. I. I. Nor Azman, M. Marzouk, and R. Al-Salahi, "Triazoloquinazolines as a new class of potent α-glucosidase inhibitors: In vitro evaluation and docking study," *PLoS One*, vol. 14, no. 8, pp. 1–13, 2019, doi: 10.1371/journal.pone.0220379.

[23] N. Kerru *et al.*, "Design, synthesis and biological evaluation of novel thiazol-2-yl benzamide derivatives as glucokinase activators," *Bioorg. Chem.*, vol. 1220, no. 2, pp. 1–20, Mar. 2018, doi: 10.1016/j.compbiolchem.2018.02.018.

[24] O. M. Antypenko, S. I. Kovalenko, and G. Zhernova, "Search for Compounds with Hypoglycemic Activity in the Series of 1-(2-(1H-Tetrazol-5-yl)-R1-Phenyl)-3-R2-phenyl(ethyl)ureas and R1-Tetrazolo[1,5-c]quinazolin-5(6H)-ones," *Sci. Pharm.*, vol. 84, no. 2, pp. 233–254, 2016, doi: 10.3797/scipharm.1507-14.

[25] A. Barmak, K. Niknam, and G. Mohebbi, "Synthesis, Structural Studies, and α-Glucosidase Inhibitory, Antidiabetic, and Antioxidant Activities of 2,3-Dihydroquinazolin-4(1 H)-ones Derived from Pyrazol-4-carbaldehyde and Anilines," *ACS Omega*, vol. 4, no. 19, pp. 18087–18099, 2019, doi: 10.1021/acsomega.9b01906.

[26] K. Javaid *et al.*, "2-Arylquinazolin-4(3H)-ones: A new class of α-glucosidase inhibitors," *Bioorganic Med. Chem.*, vol. 23, no. 23, pp. 7417–7421, 2015, doi: 10.1016/j.bmc.2015.10.038.

[27] V. Gurram *et al.*, "Design, synthesis, and biological evaluation of quinazoline derivatives as α-glucosidase inhibitors," *Bioorganic Med. Chem.*, vol. 23, no. 23, pp. 2227–2237, 2015, doi: 10.1007/s00044-014-1293-5.

[28] Y. Martynenko, O. Antypenko, I. Nosulenko, G. Berest, and S. Kovalenko, "Directed Search of Anti-inflammatory Agents Among (3HQuinazoline- 4-ylidene)hydrazides of N-protected Amino acids and their Heterocyclization Products," *Antiinflamm.*

Antiallergy. Agents Med. Chem., vol. 19, no. 1, pp. 61–73, 2019, doi: 10.2174/1871523018666190115092215.

[29] A. Sakr, H. Kothayer, S. M. Ibrahim, M. M. Baraka, and S. Rezq, "1,4-Dihydroquinazolin-3(2H)-yl benzamide derivatives as anti-inflammatory and analgesic agents with an improved gastric profile: Design, synthesis, COX-1/2 inhibitory activity and molecular docking study," *Bioorg. Chem.*, vol. 84, no. September 2018, pp. 76–86, 2019, doi: 10.1016/j.bioorg.2018.11.030.

[30] B. Dash *et al.*, "Molecular modeling, enzyme activity, anti-inflammatory and antiarthritic activities of newly synthesized quinazoline derivatives," *Bioorganic Med. Chem. Lett.*, vol. 17, no. 2, pp. 105–110, 2017, doi: 10.1111/cbdd.12454.

[31] A. A. M. Abdel-Aziz, L. A. Abou-Zeid, K. E. H. Eltahir, R. R. Ayyad, M. A. A. El-Sayed, and A. S. El-Azab, *Synthesis, anti-inflammatory, analgesic, COX-1/2 inhibitory activities and molecular docking studies of substituted 2-mercapto-4(3 H)-quinazolinones*, vol. 121. Elsevier Ltd, 2016.

[32] N. C. Cho *et al.*, "Discovery of 2-aryloxy-4-amino-quinazoline derivatives as novel protease-activated receptor 2 (PAR2) antagonists," *Bioorganic Med. Chem.*, vol. 23, no. 24, pp. 7717–7727, 2015, doi: 10.1016/j.bmc.2015.11.016.

[33] K. P. Rakesh, H. M. Manukumar, and D. C. Gowda, "Schiff's bases of quinazolinone derivatives: Synthesis and SAR studies of a novel series of potential anti-inflammatory and antioxidants," *Bioorganic Med. Chem. Lett.*, vol. 25, no. 5, pp. 1072–1077, 2015, doi: 10.1016/j.bmcl.2015.01.010.

[34] J. Hu *et al.*, "Design, synthesis, and biological evaluation of novel quinazoline derivatives as anti-inflammatory agents against lipopolysaccharide-induced acute lung injury in rats," *Chem. Biol. Drug Des.*, vol. 85, no. 6, pp. 672–684, 2015, doi: 10.1111/cbdd.12454.

[35] A. Tahghighi, S. M. Mohamadi-Zarch, H. Rahimi, M. Marashiyan, N. Maleki-Ravasan, and A. Eslamifar, "In silico and in vivo anti-malarial investigation on 1-(heteroaryl)-2-((5-nitroheteroaryl)methylene) hydrazine derivatives," *Malar. J.*, vol. 19, no. 1, pp. 1–12, 2020, doi: 10.1186/s12936-020-03269-7.

[36] A. Bouchut *et al.*, "Identification of novel quinazoline derivatives as potent antiplasmodial agents," *Eur. J. Med. Chem.*, vol. 161, pp. 277–291, 2019, doi: 10.1016/j.ejmech.2018.10.041.

[37] D. Amrane *et al.*, "Synthesis and Antiplasmodial Evaluation of 4-Carboxamido- And 4-Alkoxy-2-trichloromethyl Quinazolines," *Molecules*, vol. 25, no. 17, 2020, doi: 10.3390/molecules25173929.

[38] T. Fröhlich *et al.*, "Synthesis of Novel Hybrids of Quinazoline and Artemisinin with High Activities against Plasmodium falciparum, Human Cytomegalovirus, and Leukemia Cells," *ACS Omega*, vol. 2, no. 6, pp. 2422–2431, 2017, doi: 10.1021/acsomega.7b00310.