WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES

SJIF Impact Factor 7.421

Volume 7, Issue 4, 628-649 Review Article ISSN 2278 – 4357

A REVIEW ON QUINAZOLINONE AND ITS DERIVATIVES WITH DIVERSE BIOLOGICAL ACTIVITIES

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Article Received on
06 Feb. 2018,

Revised on 27 Feb. 2018,
Accepted on 19 March 2018

DOI: 10.20959/wjpps20184-11360

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ABSTRACT

Quinazolin-4-(3H)-one is a heterocyclic compounds, and its derivatives are synthetically important molecule, thus used for the synthesis of a large variety of compounds. The compound was first prepared condensation products of anthranillic acid and amides by Niementowski *quinazolinone synthesis*, named after its discoverer Stefan Niementowski (1866-1925). The original work was published in 1895. The first quinazoline 2-cyano-3, 4-dihydro-4-oxoquinazoline by griess at 1869. From literature survey states that most of the methods used for the synthesis of quinazolinone compounds make use of anthranillic acid or one of their functional derivatives as the starting materials. Quinazolin-4-(3H)-one is synthesized when keto group is introduced in the pyrimidine ring of quinazoline. Quinazolinone and its derivatives possess a large class of biologically active compounds that exhibited broad spectrum of biological activities such as anti-HIV, anticancer, antifungal, antibacterial, anti mutagenic, anticoccidial, anticonvulsant, anti-inflammatory, antidepressant, anti malarial, antioxidant, anti leukemic, and antileishmanial activities and other activities. Literature review state that quinazolinone derivatives have attracted strong interest in organic and medicinal chemistry due to their potent biological and pharmacological activities. The present review provides a brief overview on the recent advances and future perspectives on pharmacological aspects of quinazolinone and its derivatives reported in the last decade.

KEYWORDS: Quinazolin-4-(3H)-one, Anti oxidant activity, Anti cancer activity, Anti tubercular activity.

INTRODUCTION

These compounds have been isolated from several families in the plant kingdom, as well as from bacteria and animal species, and many are bio –synthetically derived from anthranillic acid. The first quinazoline alkaloid isolated was Vasicine (peganine) in 1888, produced by *Adhatoda vasica*. Some other quinazoline alkaloids that have been isolated, characterized, and synthesized are Chrysogine, Febrifugine, and Isofebrifugine.[1] Important classes of fused heterocyclic compound of quinazoline are found in more than 200 naturally occurring alkaloids. In plants Indol quinazolinones are mainly found in polygonum tinctorium lour, strobilanthescusia, isatistinctoria and other blue dye producing plants. In micro organisms, these compounds are isolated from fusariumlateritium nees, the marine bacterium bacillus cereus 041381, the entomopathogenic fungus isaria farinose, streptomyces sp., chaetomium species IFB-EO15, aspergillus nidulans MA-143 and penicllium aurantiogriseum.[2] The heterocyclic class of quinazoline nucleus is composed of two fused six membered aromatic rings a benzene ring and pyrimidine ring. its chemical formula C_8 H_6 N_2. Fused bicyclic compound of quinazoline earlier called as benzo-1, 3 diazine was first prepared in the laboratory in 1903 by Gabriel[3], although one of its derivatives was known much earlier.[4] based on the position of keto or oxo group it may be classified into three types: 4(3H) quinazolinone, 2(1H) quinazolinone, 4(1H,3H) Quinazolinone(5).

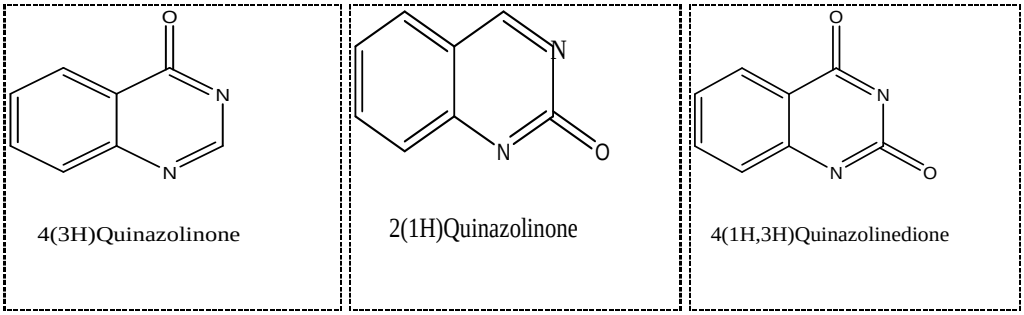


Fig. 1.

From the above (fig: 1) three Quinazolinone structures, 4(3H)- quinazolinone are most prevalent, either as natural products or as intermediates in various proposed biosynthetic pathways.[6] this is partly due to the structure being derived from the anthranillic acid or different esters,anthranilamide and anthranilonitrile, (isatoicanhydride) anthranilates while the 2(1H)-quinazolinone is predominantly a product of benzamides with nitriles or anthranilonitrile.[7]

Chemistry and chemical properties: Heterocyclic compound of quinazolinone having two structural isomers, 4-quinazolninoe and 2-quinazolinone.4-isomers are more common. Chemical name of 4-quinazolinone is found to be quinazolin-4(3H)-one or 4-oxo-3, 4-dihydroquinazoline or 4-oxoquinazolinol or (3H) quinazoline or 3, 4-dihydroquinazolin-4-one or 4-quinazolinone.Two nitrogen atoms are incorporated in chemicals with two conjoined aromatic rings, one of the carbon which is oxidized with keto oxygen. A strong lactam-lactim tautomeric interaction is present in quinazolinones.[8] this tautomeric interaction can occur when a 4(3H)-quinazolinone containing a methyl in the 3-position when chlorination with POCl3, the methyl group is lost and chlorination proceeds.[9] when the methyl group is present in the 2-position, the tautomeric effect is extended generating an exo methylene carbon. This compound can be condensed with aldehydes producing 2-styryl-4-(3H)-quinazolinone.the result of tautomeric effects, increases the reactivity effect of substituted -4-(3H)-quinazolinones.[10] hence, the quinazolinone are documented to be a "privileged structure " for drug development and discovery.[11] moreover, based on various literature, the quinazolinone ring system revealed that,[12] the positions 2,6 and 8 of the ring system much more important for structural activity studies and also chemotherapeutic activity could be increased by the inclusion of different heterocyclic moieties at position 3 of the quinazolinone ring system.[13]

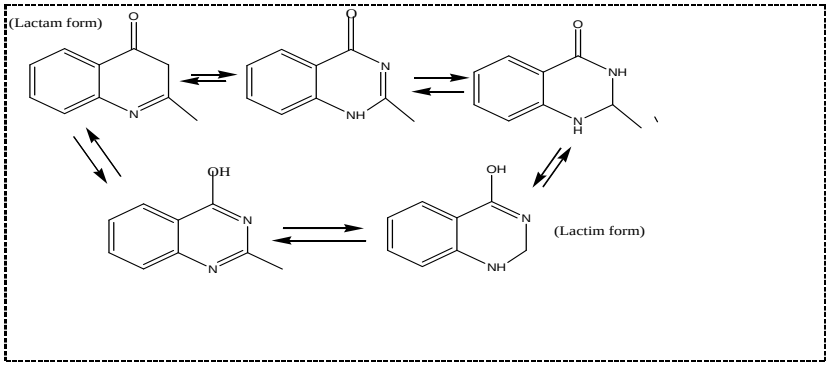


Fig. 2.

Heterocyclic compound of Quinazolinone are also a class of drugs which contain a 4-quinazolinone core have been used in the treatment of cancer. Examples are Aflaqualone[14] Ispinesib[15], nolatrexed[16], alkaloids containing quinazolinone core is febrifugine[17], halofuginone.[18]

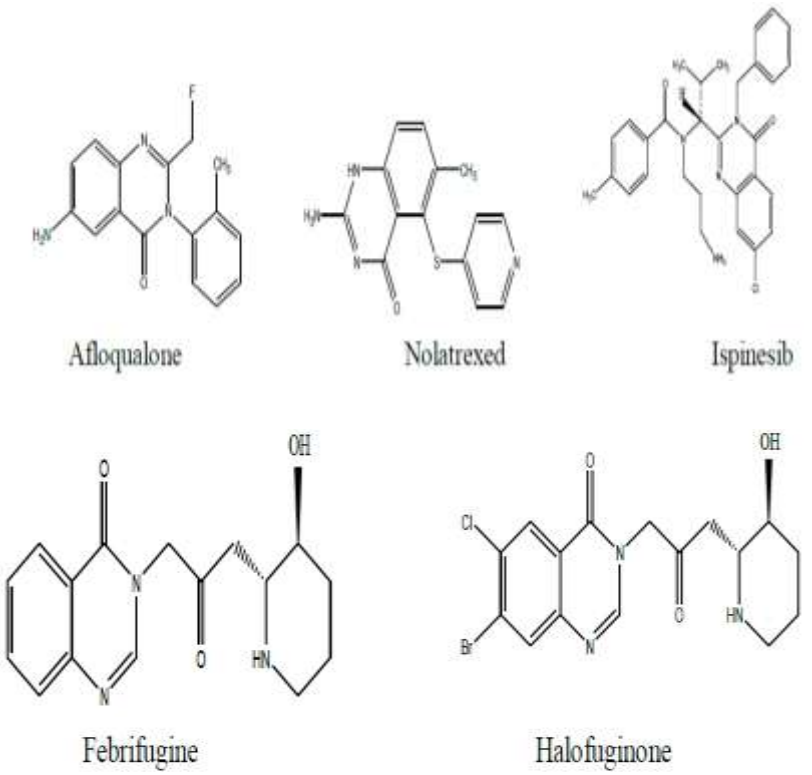


Fig. 3.

General methods for synthesis of quinazolin-4-(3H) one.

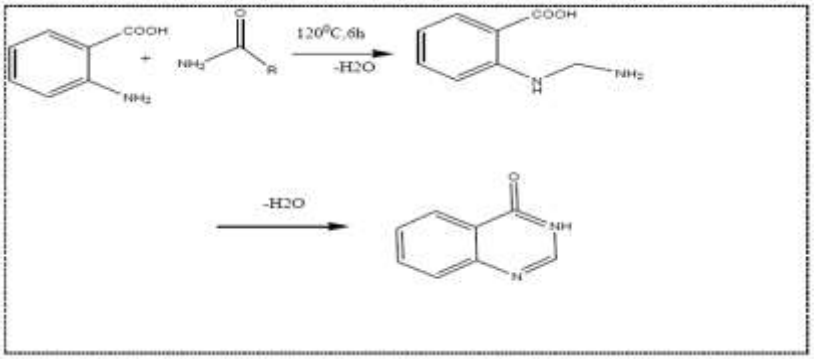


Fig. 4.

quinazolin-4-(3H)-one have been synthesized from 2 amino benzoic acid on reaction with foramide when heated at 120^0c for 6hrs.the reaction takes place with elimination of water and process through o-amido benzamides intermediate (Fig.4). This is known as Niementowski synthesis.[19]

3, 1, 4-Benoxazones react with amines to form 3, 4-dihydro-4-oxoquinazolines.primary aliphatic amines, anilines react with 2-methyl-5-nitro-4-oxoquinazolines.[20] (Fig.5).

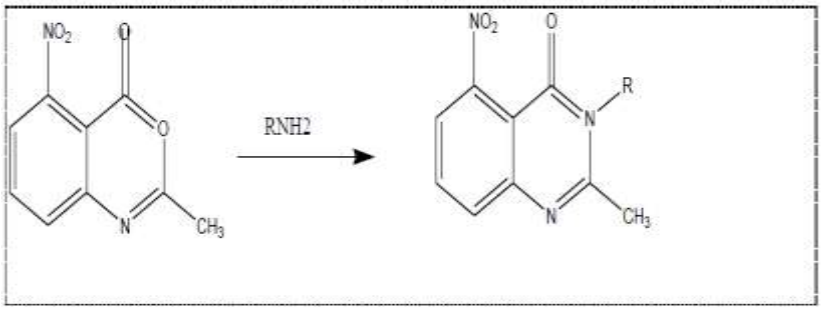


Fig.5.

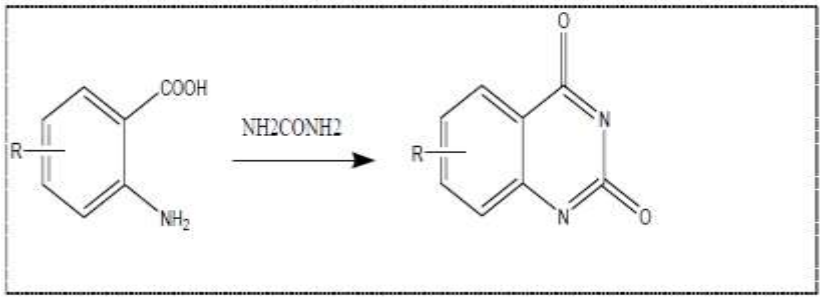


Fig.6.

Anthranillic acid fused and react with urea to produce the 1, 2, 3, 4-tertrahydro-2, 4-dioxo-quinazoline.[20] (Fig.6).

The most effective conversion of urethane derivatives. In this anilines are condensation with urethane to form a quinazolin-4-(3H)-one. The substituted 2 methyl quinazolinone derivatives was synthesized by heating urethane and acetanilide for 3hrs in the presence of phosphorous pentoxide in tolune.[19](Fig.7).

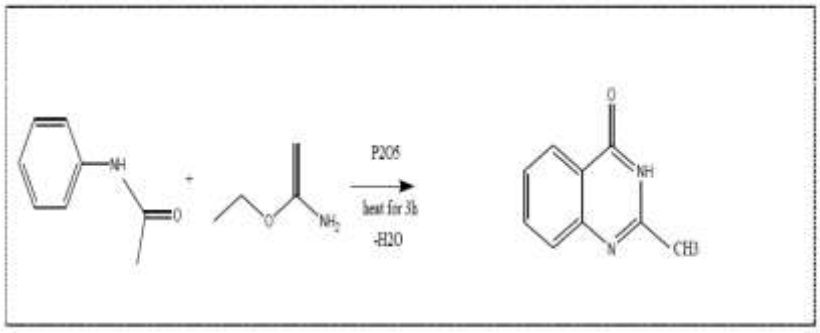


Fig. 7.

The synthesis of quinazolinone involves the reaction of N-acyl anthranillic acid by heating with ammonia or substituted amines (Fig.8)..the condensation of various primary amines and N-acyl-5-nitroanthranilic acid to form the 2-methyl-3-aikyl-6-nitro-quinazolin-4-(3H)-one in good yield.[20]

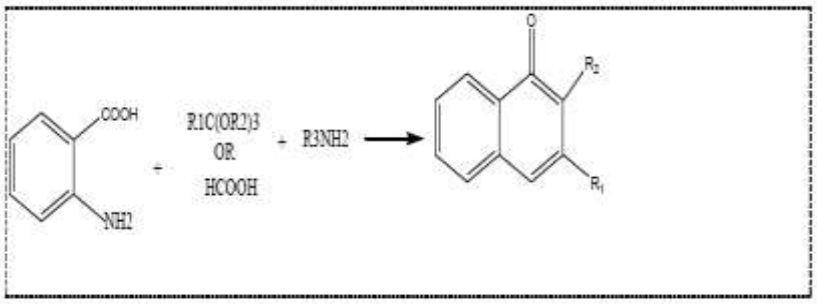


Fig. 8.

Medicinal importance of quinazolinone derivatives

Anti microbial activity

Kunwar et al[21], *Synthesis of 1, 2 di substituted quinazolinone derivatives have been synthesized using aniline and aldehydes derivatives by ulman condensation reaction were reported..The synthesized compounds have been established on the basis of spectral analysis (IR, NMR).Investigation a microbial property against S.aureus, P.arguginosa, and E.coli by standard disk method using standard drugs, cefriaxone.it has been observed that all the compounds showed good activity because of the presence of groups like* CH_3,-NH_2-,-F-,-S-C_6H_5 *at the different position of phenyl molecule of quinazolinone as compared with standard drug.*

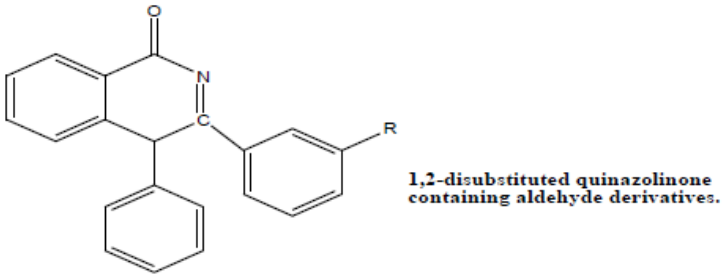
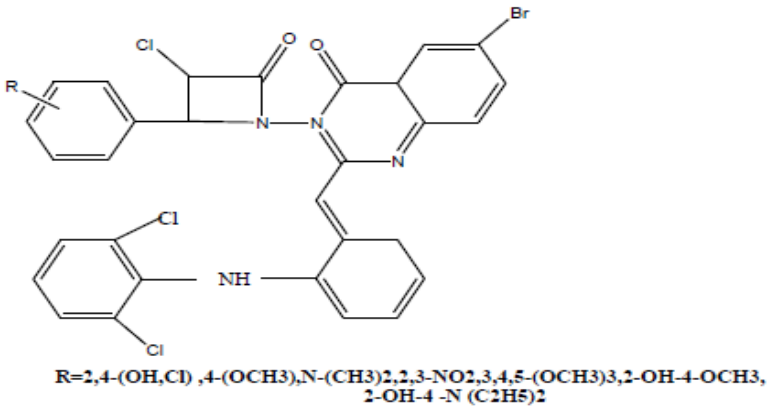


Fig. 9.

Navin et al[22]*, A series of 2-oxo-azetidinyl-quinazolin-4(3H)-ones and diclofenac analogue have been synthesized from condensation reaction with substituted aromatic aldehydes to form Schiff bases by cyclisation reaction of acid chloride with bromo anthranillic acid to form benzoxacine 4 one. further reaction of benzoxazinone with hydrazine hydrate. The structures of synthesized compounds were elucidated on the basis of elemental analysis as well as IR, NMR spectral data. The synthesized compounds were screened for bacterial, fungal activities having good activity of chloro and methoxy containing compounds.*



R=2,4-(OH,Cl) ,4-(OCH3),N-(CH3)2,2,3-NO2,3,4,5-(OCH3)3,2-OH-4-OCH3, 2-OH-4 -N (C2H5)2

Fig. 10.

Trilok Chandra et al[23], *synthesis of novel and potent anti inflammatory activity of sulpha drug quinazolin-4-one derivatives were reported. a mixture of 6-bromo-2-methyl-quinazolin-4-one and sulphathiazole was dissolved separately in methanol (25ml) by warming obtained 6-bromo-2-methyl-N-(thiazol-2-yl/pyrimidin-2-yl-benzenesulfonamide)quinazolin-4(3H)-ones.this compound on bromination in glacial acetic acid to form the 6-bromo-2-(bromo methyl)-N-(thiazol-yl/pyrimidin-2-yl-benzenesulfonamide)quinazolin-4(3H)ones.further, on reaction with hydrazine hydrate to produce the 6-bromo-2-(hydrazinylmethyl)-N-(thiazol-2-yl/pyrimidin-2-yl-benzenesulfonamide)quinazolin-4(3H)-ones.this compound react with substitutedaldehyde to form the 6-bromo-2-(substituted benzylidene hydrazinyl) methyl)-N-(thiazol-2-yl/pyrimidin-2-yl-benzene sulfonamide)quinazolin-4-(3H)-ones. 6-bromo-2-(substituted benzylidene hydrazinyl) methyl)-N-(thiazol-2-yl/pyrimidin-2-yl-benzene sulfonamide)quinazolin-4-(3H)-ones react with chloroacetyl chloride in the presence of triethyl amine to form the 6-bromo-2-()3-chloro-2-oxo-4-phenylazetidin-1-ylamino)methyl)-N-(thiazol-2-yl/pyrimidin-2-yBenzene sulfonamide) quinazolin-4-(3H)-ones. 6-bromo-2-(substituted benzylidene hydrazinyl) methyl)-N-(thiazol-2-yl/pyrimidin-2-yl-benzene sulfonamide)quinazolin-4-(3H)-ones react with thioglycolic acid in the presence of anhydrous zinc chloride to form the 6-bromo-2-(-4-oxo -2 -phenylthidiazolidin-3-ylamino)methyl)-N-(thiazol-2-yl/pyrimidin-2-yl benzene sulfonamide)quinazolin-4-(3H)-ones.all the synthesized compounds exhibited anti inflammatory activity and analgesic activity at the dose 50mg/kgp.o.the structure of all the synthesized compounds were elucidated by spectral (IR,H NMR) and elemental (C,H,N) analysis.*

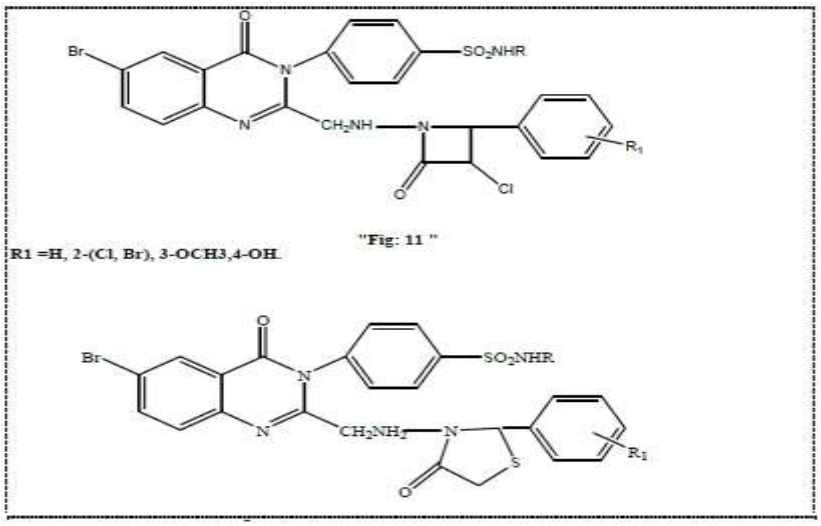


Fig. 12.

Renee bouley et al*[24]*, *Newly synthesized quinazolinone derivatives, anthranillic acid were cyclised by heating in triethyl orthoacetate,and, and the solution was cooled to -20^{0}C to crystallize intermediate compound benzoxazinone in high purity. This compound was dissolved in glacial acetic acid by heating, substituted aniline is added, and the mixture was allowed to reflux for 4-6 hrs to form quinazolinone compounds. In this various aldehydes were allowed to react in the presence of acetic acid to form the different quinazolinone derivatives. Reported, the first structure activity relationship of this class of anti bacterial by systematically varying the quinazolinone structure in rings 1,2 and 3(figure).each derivative was screened for in vitro antibacterial activity by determining MICs against our panel of bacterial strains and specifically improve the activity for S.aureus.several derivatives that displayed good activity in vitro were selected for testing for in vitro toxicity, pharmacokinetic (PK) properties in mice, and efficacy in mouse models of infection. This new quinazolinone has potent activity against methicillin –resistant (MRSA) strains, low clearance, and oral bioavailability and shows efficacy in a mouse neutropenic thigh infection model.*

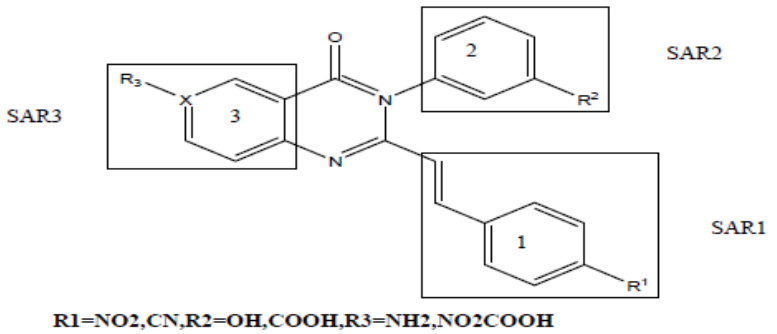
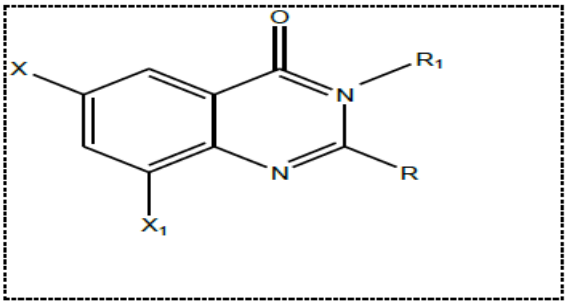


Fig. 13.

Anti oxidant activity

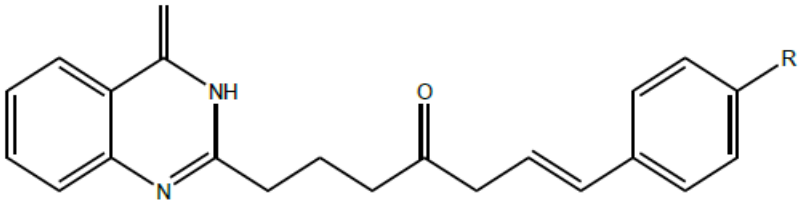
Govindaraj et al[25], *Synthesis and evaluation of anti oxidant activities of some novel quinazolinone derivatives were reported. a novel quinazolin-4-(3H)-one were synthesized by condensation of 2-amino-4-phenylthiazole/2-amino-3-carbethoxy-4,5,6,7-tetrahydrobenzothiophene with 6,8-(un/mono/di)-bromo-2-(methyl/phenyl)-4H-benzo-(1,3)-oxazine-4-ones. 2-amino-4-phenylthiazole and 2-amino-3-carbethoxy-4,5,6,7-tetrahydrobenzothiophene were synthesized from acetophenone and cyclohexanone.the 6,8-(un/mono/di)-bromo-2-(methyl/phenyl)-3H-benzo-(1,3)-oxazine-4-ones were synthesized from 3,5-(un/mono/di)-bromo anthranillic acid. The chemical structures of the synthesized compounds were confirmed by means of IR, 1HNMR and mass spectral, elemental analysis. These compounds were screened for anti oxidant activity by DPPH radical scavenging activity.*



R_1=C_9H_6NS,$C_{11}H_{13}O_2S$.R=CH_3,C_6H_5.X_1=H, Br.X=H, Br

Fig. 14.

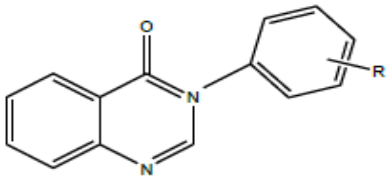
K.P.Rakesh at el[26], *A series of Schiff's bases of quinazolinone derivatives were reported to posses the potential anti inflammatory and anti oxidant activity with SAR studies.* The present study deals with the synthesis of Schiff bases by reacting quinazolinone hydrazides in the presence of glacial acetic acid. The all the newly synthesized including intermediates were confirmed by IR, HNMR, CNMR and mass spectral analysis. All the compounds were evaluated in vitro anti oxidant activity with standard drug like commercial ascorbic acid,gallic acid,butylated hydroxyl toluene,butylated hydroxyl anisole(BHA) by DPPH & ABTS DMPD radical scavenging activity, also evaluated for their in vitro anti-inflammatory activity using known literature procedure in human erythrocytes with standard drug aspirin. The compounds containing electron donating group like OH, OCH_3 better strong radical scavenging activity than other compounds. The compounds containing electron withdrawing group like Cl, NO2 excellent activity and few of them showed moderate anti inflammatory activity.



(R=Cl, NO2, OH, OCH3)

Fig. 15.

Ghana rubha et al[27], A series of novel quinazoline-4-(3H)-ones were synthesized and in vitro anti inflammatory activity of synthesized compounds were studied using protein by bovine serum albumin(BSA) and compared with standard ibuprofen.3-(4-bromo phenyl)-4-(3H) quinazolinone, 3-(-4-methyl phenyl)-4-(3H) quinazolinone exhibited highest invitro anti inflammatory activity among the synthesized compounds. The anti oxidant capacity of quinazolinone were studied using different invitro analytical methodologies such as 1,1 diphenyl -2-picryl-hydrazyl free radical (DPPH) scavenging, total reducing ability determination using Fe^{3+},Fe^{2+} transformation method, nitric oxide scavenging & hydrogen peroxide scavenging, were used as the reference anti oxidant radical scavenger compounds.3-(-4-bromo phenyl)-4-(3H) quinazolinone,3-(2,6dimethyl phenyl)-4-(3H)quinazolinone,3-(4-methyl phenyl)-4-(3H) quinazolinone exhibited highest scavenger activity among the synthesized compound. In addition methylated compound exhibited better activity from the synthesized compounds. Quinazoline 4-3H –ones were synthesized and characterized by IR, H^1 NMR and mass spectral analysis.



R= derivatives of aromatic amines

Fig. 16.

Anti tubercular activity

Meenu chaudhary et al[28], *A series of novel substituted (1, 2, 4) triazolo (1,5c) quinazolinone derivatives were synthesized by mannich reaction using foramide and different secondary amines. Structures of compounds were confirmed by IR, H-NMR and mass spectroscopic analysis. The anti tubercular activity of synthesized compounds was performed*

against M.tuberculosis H37Rv at concentration 30µg/ml using streptomycin and pyrazinamide 7.5µg/ml as standard drug. All the synthesized compounds have shown anti-tubercular activity as compared to standard drug. compounds (Fig.17) has shown very good anti tubercular activity.

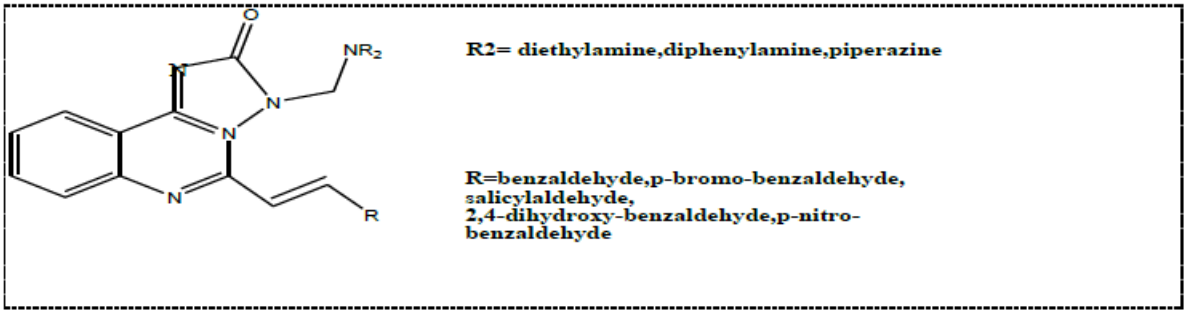


Fig. 17.

***Kalpnana Devi et al[29]**, Synthesis and anti tubercular activity of some new 2-3-disubstituted quinazolinone were reported. Nicotinic acid and thionyl chloride were refluxed for 2hrs to form the nicotinyl acid chloride which was added drop wise into the solution of anthranillic acid in dry pyridine to form 2-(pyridine-2-yl)-4H-benzo(d)(1,3)oxazin-4-one).this compound react with hydrazine hydrate to form the 3-amino-2-(pyridine-2-yl) quinazolin-4(3H)one. This compound react with2-(secondary amino (morpholine))-acid chloride in the presence of dry pyridine to form the 2-(substituted)-N-(4-oxo-2-pyridin-2-yl-4H-quinazolin-3-yl)-acetamide derivatives. All the synthesized compounds were screened for invitro ant tubercular activity by MABA method against mycobacterium tuberculosis and it was found that almost all the compounds have exhibited moderate activity (MIC at 50µg/ml) as compared to standard drugs which have shown activity at 3.125µg/ml.the structure of all the synthesized compounds was confirmed by IR, NMR, and mass, CHN spectral data.*

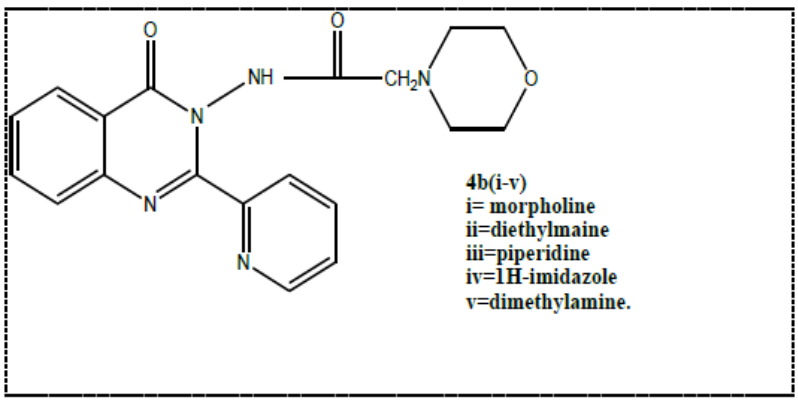
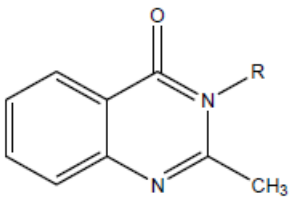
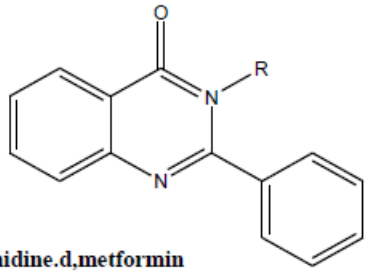


Fig. 18.

KK Rajasekhar et al[30], *newly synthesized anti tubercular and anti bacterial activity of quinazolinone derivatives were reported. Fourteen compounds that belongs to either 2-methyl substituted quinazolinone or 2-phenyl substituted quinazolinone were synthesized. from seven methyl substituted derivatives 5 compounds showed a minimum inhibitory concentration value between 6.25 and 100µg/ml against mycobacterium tuberculosis except phenyl hydrazine substituent and phenyl substituted quinazolinone derivatives 3 compounds showed minimum inhibitory concentration especially urea and thio urea substituent. The use of amido, thioamido, imidamido, N, N-dimethyl guanidinyl, or N-pyridoyl substituent at 3-position of quinazolinone was found to increase anti tubercular activity. A binding affinity prediction by auto dock vina was higher for the 2-phenyl series, which may be due to increased hydrophobic interactions within the binding site of enoyl-acyl carrier protein reductase.*



"*Fig: 19*"



R,a = urea,b.thio urea.c,guanidine.d,metformin e=isonicotinic hydrazide,f=phenyl hydrazine g=2,4-dinitrophenyl hydrazine.

"*Fig: 20*"

Anti cancer activity

AAF. Wasfy at el[31], *Synthesis and anti-cancer properties of novel quinazoline derivatives were reported. The results revealed that some of the synthesized compounds have a signicant biological activity as anti cancer agents. a novel quinazoline were synthesized by reaction of 5-chloroanthranilic acid with isonicotinyl chloride in dry pyridine to form 5-chloro-2-(isonicotinamido) benzoic acid. Cylocodensation of 5-chloro-2-(isonicotinamido) benzoic acid with acetic anhydride to form 6-chloro-2-(pyridine-4-yl)-4H-benzo(d)(1,3)oxacin-4-one. Interaction of 5-chloro-2-(isonicotinamido) benzoic acid with ammonium acetatein the presence of ammonium hydroxide in sand bath to produce 6-chloro-2-(pyridine-4-yl)quinazolin-4(3H)-one.the reaction of 6-chloro-2-(pyridine-4-yl)-4H-benzo(d)(1,3)oxacin-4-one with phosphorous pentachloride to form 6-chloro-4-chloro-2-(pyridine-4-yl)quinazoline. Interaction of 6-chloro-4-chloro-2-(pyridine-4-yl) quinazoline with p-amino*

acetophenone in pyridine to form 1-(4-(6-choloro-2-(pyridine-4-yl) quinazolin-4-ylamino) phenyl) ethanone.1-(4-(6-choloro-2-(pyridine-4-yl) quinazolin-4-ylamino) phenyl) ethanone reacted with different aldehydes. certain new quinazoline derivatives(3,4,5,6b,6d,8b,8d) were synthesized, characterized and subjected to a screening system for evaluation of anti tumor activity against liver cancer (HEPG2) tumor cell line. The anti tumor activity results indicated that the selected quinazoline derivatives showed anti tumor activity against liver cancer tumor cell line tested but with varying intensities in comparison to the known anti cancer drug:doxorubicin.compounds (6b,8d) exhibited a strong growth inhibition activity against liver cancer (HEPG2) on the tested tumor panel cell line in comparison to the standard drug. The newly synthesized compounds were characterized by IR, NMR analysis. All newly synthesized compounds were screened for their anti cancer studies.

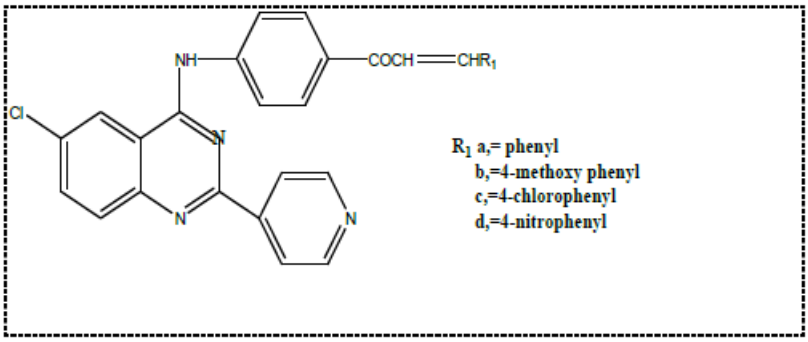


Fig. 21.

Zahoor et al[32], *Anticancer activity of a novel quinazolinone-chalcone derivative were reported. The condensation of anthranillic acid with acetic anhydride to form the benzoxazinone. benzoxazinone was coupled with 3-amino acetophenone to produce the quinazolinone. this quinazolinone was made to undergo condensation reaction with substituted benzaldehydes in presence of a base to afford the desired quinazolinone –chalcone derivatives.anti cancer activity determined through MTTassay,colony formation assay, wound healing assay, cell cycle and western blot analysis in mia paca-2 cells treated with quinazolinone –chalcone derivatives. The findings are indicative of synthesized compounds exerting anti cancer activity through cell cycle arrest at G2/M phase and not through apoptosis. Reduction in the motility of mia paca -2 cells indicates anti-metastatic potential of quinazolinone-chalcone derivatives.*

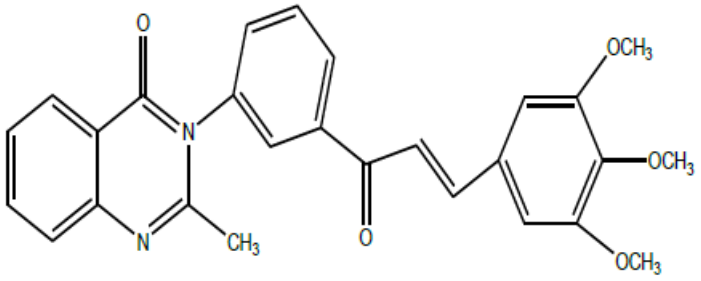


Fig. 22.

***Hatem A et al*[33]**, *A new series of anti cancer activity of quinazoline derivatives was synthesized, characterized via physiochemical and spectral means and reported. Treatment of 2-amino -5-methyl benzoic acid with butyl isothiocyanate resulted in the new 2-thioxoquinazolin-4-one.alkylation and hydrazinolysis of 2-thioxoquinazolin-4-one thio ether and hydrazine derivatives and then was further transformed into tricyclic derivative via Cylocodensation reaction. The cytotoxicity of all compounds was evaluated in vitro against the Hela and MDA-MB231 cancer cell lines using MTT assay. The treatment of the cells was performed with the synthesized compounds and gefitinibat at 0,1,5,10,25 and 50µM and incubated for 24hrs in 50% DMSO. the IC_{50} values of the target compounds were reported in µM using gefitinibat as a standard. All the compounds exhibited in vitro cytitoxic activity against both cell lines.thioxo group showed good activity and thio ether derivatives were found to be more potent than geftinib.thus compounds may be potential anti cancer agents that probably act via the EGFR-TK pathway.*

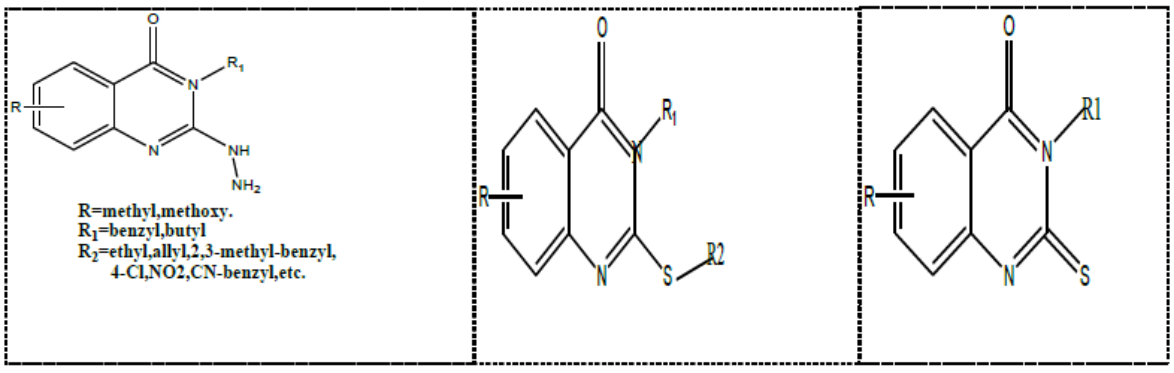


Fig: 23 ***Fig: 24*** ***Fig: 25***

***Sapavat Madhavi et al*[34],** *Anti cancer activity of novel chalcone incorporated quinazolinone derivatives were reported. A mixture of anthranillic acid with foramide in ethanol to form the*

quinazolin-4-ol.this compound was dissolved in 50ml of $POCl_3$ heated on an oil bath at 120^oC for 4 hrs to form produce the 4-chloroquinazoline then which were dissolved N-methylpyrrolidine and 4-aminobenzaldehyde and heated at 60^0c, added 4 drops of HCl heated at 1hr to form the 4-(quinazoline -4-ylamino) benzaldehydes. 4-(quinazoline -4-ylamino) benzaldehydes react with halogen substituted acetophenone in the presence of piperidine and ethanol reflux for 4hrs to form final compound of chalcone containing quinazoline derivatives. All the synthesized compounds evaluated for their anti cancer activities against four human cancer cell lines (A549,HT-29,MCF-7,A375) from ten four compounds showed potent anticancer activity than standard drug of combretastatin-A4 by using MTT assay.

Fig. 26.

Biswajit Dash et al*[35]*., *The present study designed to synthesize some new, In vivo antitumor activity of novel 3, 4 di-substituted quinazoline derivatives were reported. A new series of 7-chloro-3-(substituted (amino/phenyl amino)) -phenyl quinazoline-4-(3H)-one/thione derivatives and 1-(7-chloro-4-oxo/-2-phenylquinazoine-3 (4H-yl) - substituted urea derivatives were synthesized. The reaction proceeds through 7-chloro-2-henyl-4H-benzo (d) (1, 3) oxazin-4-one acting as intermediate product. The in vivo antitumor activity of synthesized quinazoline derivatives was evaluated by body weight analysis; mean survival time and percentage increase in life span methods in Swiss albino mice bearing ehrilich as cites carcinoma. From this research which indicates that amino group at position 3, urea, thiourea group in phenyl hydrazine ring in position 3of quinazoline scaffold crucial for anti tumor activity. All the newly synthesized compounds were characterized by IR, H^1 NMR and mass spectra, elemental analysis.*

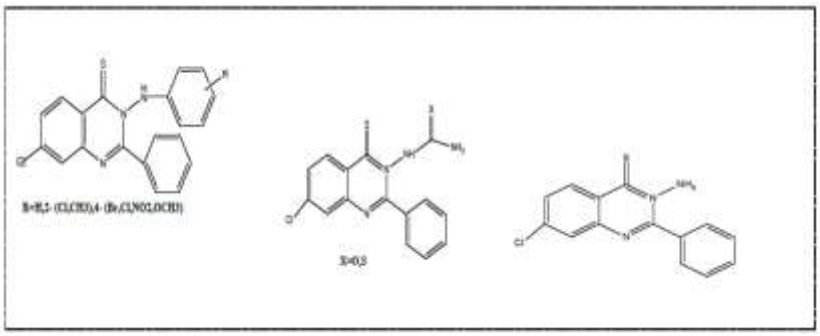


Fig. 27.

Leila Hosseinzadeh at el[36]*., cytotoxic evaluation of some new series 3-(2-(2-phenylthiazol-4-yl) ethyl)-quinazolin-4(3H) one derivatives, synthesized and reported. The newly synthesized quinazolinone by the reaction of 4-ethyl-2-phenylthiazole and benzoxacinone.all the synthesized compounds were tested against three human carcinoma cell lines including MCF-7, HT-29, PC-3 by MTT assay. Compounds A3, A2, B4, and A1 showed highest cytotoxic activities against PC-3 cell line. From this research, substitution on position 6 was not beneficial cytotoxic acticity.the purity of the compounds was confirmed by thin layer chromatography using various solvents. The structure confirmed by IR, H NMR and mass spectral analysis.*

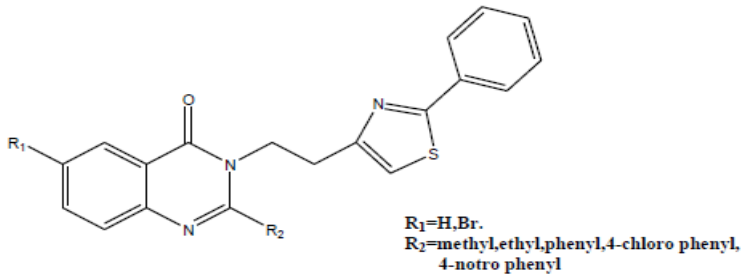
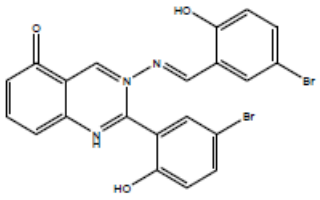
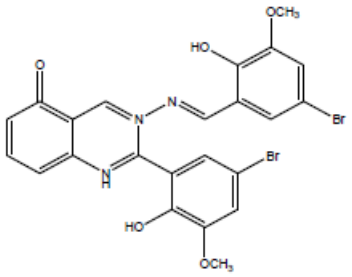


Fig. 28.

Fadhil lafta faraj et al[37]*, anti cancer activity of new quinazolinone derivatives synthesized and reported. The newly synthesized quinazoline Schiff bases were investigated for anti cancer activity against MCF-7 human breast cancer cell line. The structures were confirmed by elemental analysis, spectroscopic techniques, and x-ray diffraction studies. These compounds shown anticancer potential against MCF7 breast cancer cells and also compounds possess the capacity of inducing intrinsic and extrinsic apoptosis pathway, which was well regulated by caspase enzymes. The active role of mitochondria in the cell death was confirmed by reducing the MMP, release of cytochrome c, and ROS elevation. The newly synthesized compounds exhibited promising anti cancer agents.*

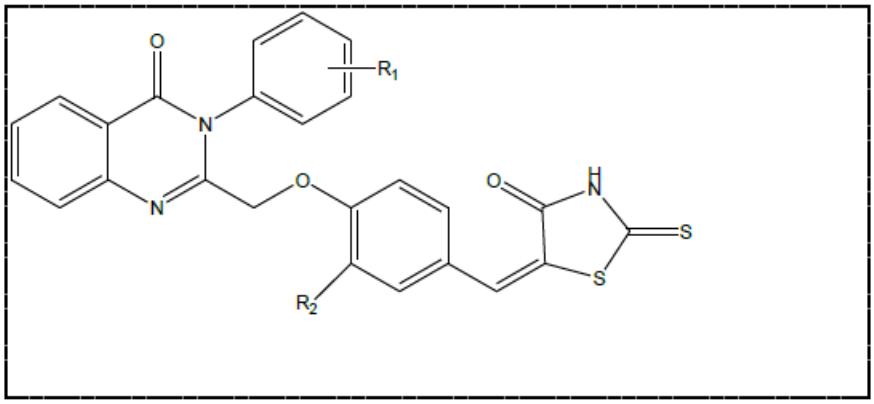


"Fig:29"



"Fig:30"

Sheridan El-Sayed et al[38] Anti cancer activity of novel quinazolinone-based rhodanines synthesized were reported. a novel series of twenty quinazolinone based rhodanines were synthesized via Knoevenagal condensation between 4-(3-(substituted phenyl)-3,4-dihydro-4-oxoquinazolin-2-yl)methoxy)substituted benzaldehydes and rhodanine.the newly synthesized compounds were evaluated invitro cytotoxic activity against the human fibro sarcoma cell line HT-1080 as a preliminary screen using MTT assay. Structure –activity relationship of the tested compounds revealed that bulky, hydrophobic, electron withdrawing substituents at Para position of the quinazolinone 3-phenyl ring increase the cytotoxicity and methoxy group on the central benzene ring was also positive impact on cytotoxicity. Elemental and spectral analyses were used to confirm the structures of the newly synthesized compounds.



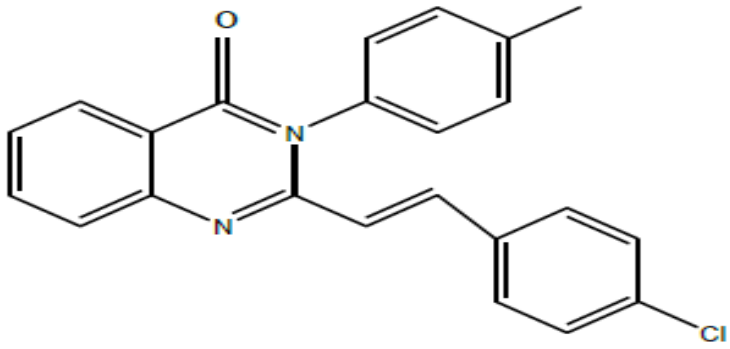
(R_1=CF_3, Cl, Br) (R_2=H, OCH3)

Fig. 31.

Anti leishmanial activity

Yihenew Simegniew Birhan et al[39], Antileishmanial evaluation of some 2, 3-disubstituted-4(3H)-quinazolinone derivatives were synthesized and reported. The target compounds were synthesized by using anthranillic acid as the starting compound and cyclisation, condensation, hydrolysis reactions. Most of the synthesized compounds better antileishmanial

activity as compared to standard drug miltefosine (IC_{50} =3.11911µg/ml).(E)-2-(4-chlorostyryl)-3-p-tolyl-4(3H)-quinazolinone exhibits the most promising antileishmanial activity when compared to standard drugs amphotericin B deoxychloate and miltefosine.the structures of the synthesized compounds were confirmed by elemental analysis, IR, and H^1 NMR. Thus 2, 3 –disubstituted -4-(3H)-quinazolinone containing an aromatic substitution at position 3 and styryl moiety at 2 position exhibiting a promising matrix for the development of antileishmanial agents.



(E)-2-(4-Chlorostyryl)-3-p-tolylquinazolin-4(3H)-one

Fig. 32.

V.Navale et al[40], Synthesis of some novel heterocyclic Schiff bases of quinazoline derivatives were reported, the starting 3-amino-2-methyl-3H-quinazolin-4-one were prepared by the reaction of 2-amino benzoic acid with acetic anhydride to form 2-Methyl-benzo(d)(1,3)oxacin-4-one,which react with hydrazine hydrate by condensation to form the 3-amino-2-methyl-3H-quinazolin-4-one, which on further condensation with substituted acetophenone in presence of acetic acid to form the imines. The structure of newly synthesized imines were confirmed by the spectral analysis (IR,H^1 NMR)therefore all the synthesized compounds exhibited satisfactory spectral data consistent with their structures.

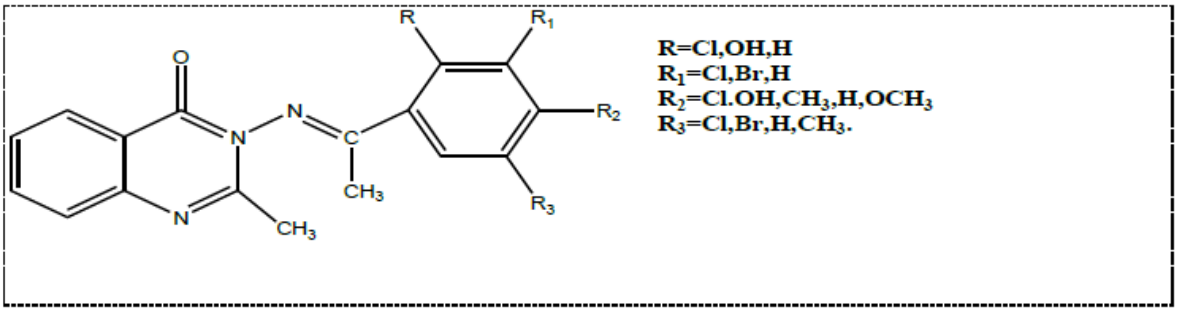
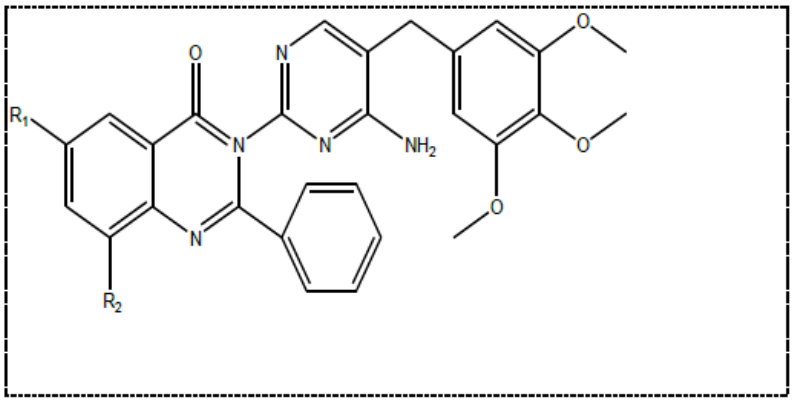


Fig. 33.

P.Selvam et al[41], A series of novel 2, 3-disubstitutedquinazolin-4(3H)-ones were synthesized and reported. The newly synthesized compounds by Condensation of 2-substituted benzo (1,3) oxazine-4-ones and primary aromatic amino group of sulphonamide derivatives. Their chemical structure were confirmed by spectral analysis(FT-IR and H^1NMR).synthesized compounds were screened for in vitro antiviral activity against HIV-1 and -2 replication in MT-4 cells. Cytotoxicity were investigated in uninfected MT-4 cells(C-type Adult T Leukemia cells).all the synthesized compounds exhibited cytotoxicity in MT-4 cells (CC_{50}:1.93-87 µg/ml) and compound SPB-111 displayed marked cytostatic properties in MT-4 cells (CC_{50}:1.93±0.29µg/ml).



(R_1=H,R_2=H),(SPB-III)

Fig. 34.

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