Acta Scientific Pharmaceutical Sciences (ISSN: 2581-5423)

Volume 9 Issue 2 February 2025

Review Article

Recent Advances in Quinazoline Derivatives: Synthesis, Biological Activities, and Therapeutic Potential

Priyanka*, Priyanshu, Monika and Sharma Madhu Suresh Kumar

Department of Pharmacy, AKTU, Lucknow, India

***Corresponding Author:** Priyanka, Department of Pharmacy, AKTU, Lucknow, India.

Received: January 15, 2025

Published: January 31, 2025

Abstract

Among heterocyclic compounds, quinoline is an advantage that appears as a significant assembly motive for the development of new drug entities. Quinoline and its derivatives tested with diverse biological activity constitute an important class of compounds for new drug development. Therefore, many scientific communities have developed these compounds as intent structure and evaluated their biological activities. The present, review provides brief natural sources of quinoline and including a new extent of quinoline-based marketed drugs. This review also confers information about the biological activities of quinoline derivatives such as antibacterial, antifungal, antimycobacterial, antiviral, anti-protozoal, antimalarial, anticancer, cardiovascular, CNS effects, antioxidant, anticonvulsant, analgesic, anti-inflammatory, anthelmintic and miscellaneous activities.

Keywords: Anti-Virus; Anti-Tuberculosis; Anti-Oxidation

Introduction

Heterocycles containing nitrogen atom are an important category of the favourable structures in the field of medicinal chemistry [1]. Quinazoline has been taken for this review, as quinazoline has a very broad spectrum of pharmacological activities with minimum side effects [2].

Researchers have already determined many therapeutic activities of quinazoline derivatives, including anti-cancer [3-6], anti-inflammation [7,8], anti-bacterial [8-10], analgesia [7,9], anti-virus [11], anti-cytotoxin [12], anti-spasm [9,13], anti-tuberculosis [14], anti-oxidation [15], antimalarial [16], anti-hypertension [17], anti-obesity [18], anti-psychotic [19], anti-diabetes [20], etc.

Structure activity relationship studies of quinazolinone derivatives in various literatures have revealed that substitution at positions 2 and 3, existence of halogen atom at 6 and 8 positions and substitution (mainly amine or substituted amine) at 4th position of the quinazolinone ring can improve their antimicrobial activities [21-24].

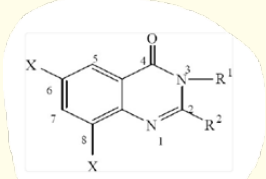
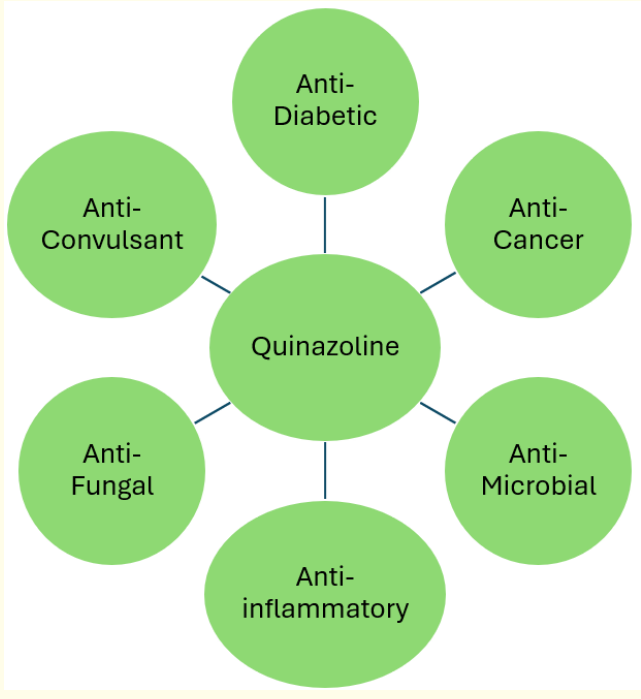


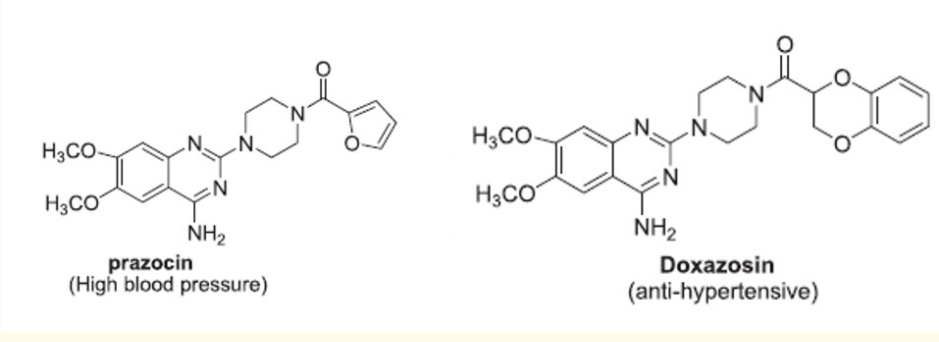
Figure 1

Several quinazoline derivatives are approved drugs, such as Terazosin hydrochloride, Prazosin hydrochloride and Doxazosin mesylate [25] (Figure). Moreover, due to the promising therapeutic efficacy against human cancers, various quinazoline derivatives like Erlotinib [26].

Approved marketed drugs with quinazoline structure

Most of these approaches use the Niementowski reaction, which fuses the analogues of anthranilic acid with amides (Scheme 1) at temperatures between 130 and 150 °C via the formation of an o-amidobenzamide intermediate [27].


Anti-
Diabetic
Anti-
Convulsant
Anti-
Cancer
Quinazoline
Anti-
Fungal
Anti-
Microbial
Anti-
inflammatory


prazocin
(High blood pressure)
Doxazosin
(anti-hypertensive)

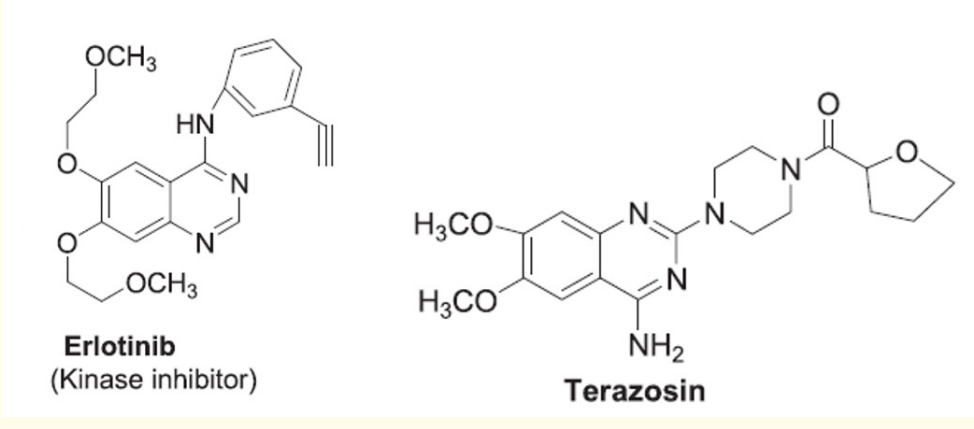
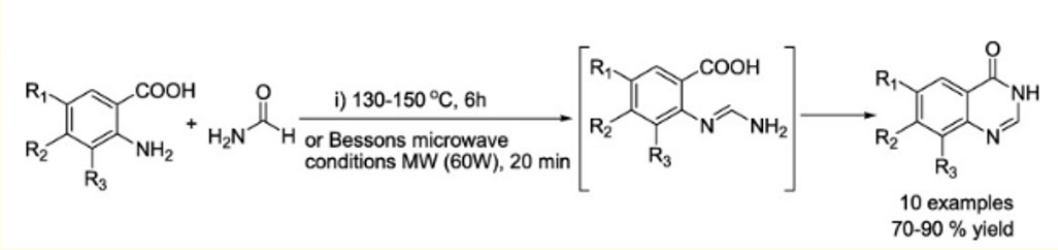

Erlotinib
(Kinase inhibitor)
Terazosin

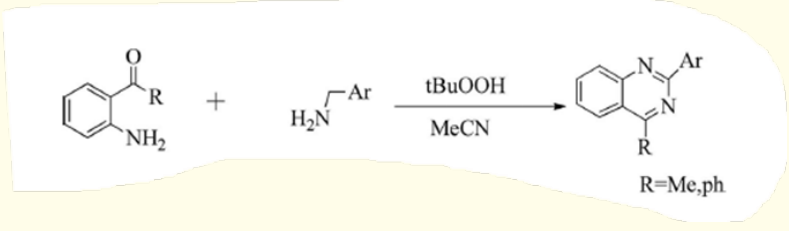
Figure 2



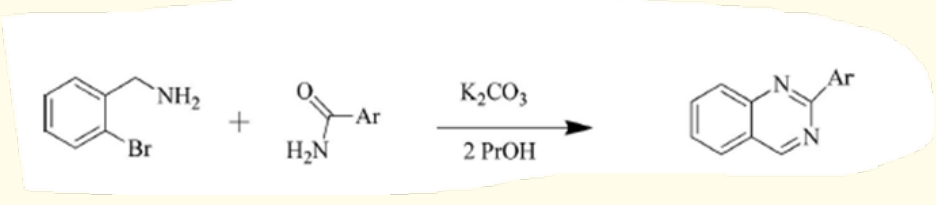
Scheme 1: Synthesis of quinazoline by Niementowski reaction or by Besson's microwave conditions.

Hydroperoxide in acetonitrile 2-aminobenzophenones and benzylic amines yields quinazoline derivatives. [28].

Quinazoline derivatives are prepared by reaction of 2-bromophenyl methyl amines and amindes catalyzed by ligand free copper (Scheme 3) [29].



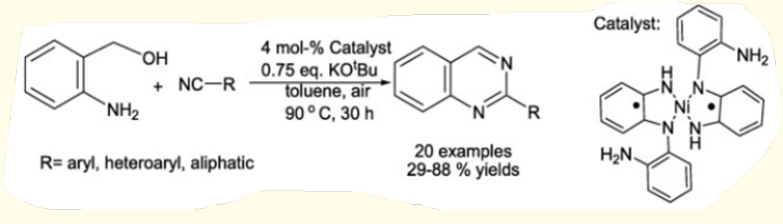
Scheme 2: Synthesis of 2-phenyl quinazoline.



Scheme 3: Synthesis of 2-aryl quinazoline.

Paul and coworkers [30] recently reported reaction of nitriles with 2-aminobenzyl alcohol for the preparation of quinazolines in good yields, by means of a biomimetic dehydrogenative condensation/coupling process Scheme 4.

Sarma and Prajapati reported a catalyst- and solvent-free synthesis of quinazoline derivatives 20 from aldehydes 18, 2-aminobenzophenones 19, and ammonium acetate under microwave heating conditions (Scheme 5).



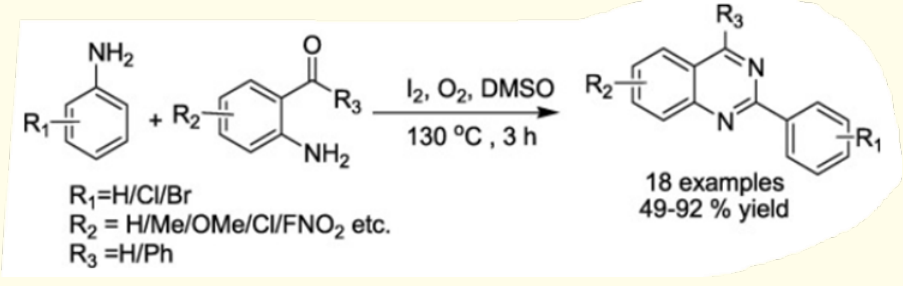
Scheme 4: Singlet diradical diamine Ni (II) catalysed the synthesis of aryl quinazolines.

Scheme 5: Reaction of aldehydes and 2-aminobenzophenones under microwave heating conditions.

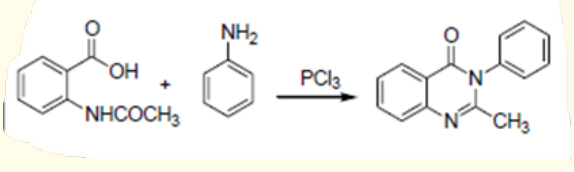
The synthesis of quinazoline derivatives by the 2-aminobenzaldehydes or 2-aminobenzophenones with benzyl- amines was recently published by Bhanageet., *et al*. [32] Using a set of samples of functionalized 2-aminobenzaldehydes or 2-aminobenzophenones, numerous functionalized hetero- aryl or aryl amines were studied to produce quinazolines in yields of 49-92% (Scheme 6).

Morgan's method for the synthesis of quinazoline (Scheme 2) involve the reaction between 2 acetamido benzoic acid and an amine in the presence of phosphorous trichloride to produce 2-methyl-3-phenylquinazolin-4(3H) one (Scheme 7) [33,34].

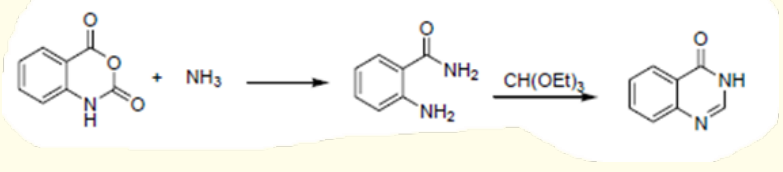
The reaction between isotopic anhydride and an amine, followed by refluxing with ethyl orthoformate (Scheme 3) produces 4-(3H)-quinazolinone [35].



Scheme 6: Molecular iodine catalysed reaction of benzyl-amines with 2-amino benzophenones or 2-aminobenzaldehydes.

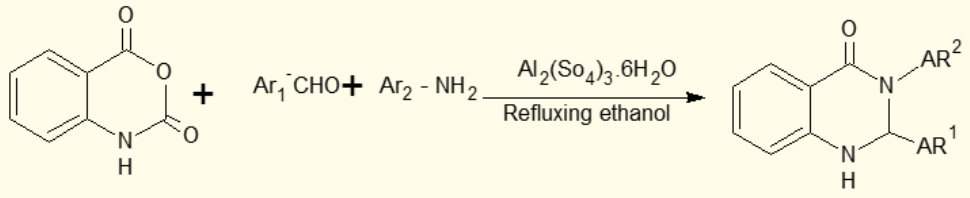


Scheme 7: 4-quinazolineone by Morgan's method.



Scheme 8: Synthesis of 4-quinazolinone.

Alireza Barmak., *et al*. [36] synthesized 2,3-dihydroquinazolinones by the reaction between aromatic aldehydes (2) and isatoic anhydride with aniline derivatives (3) and investigated under optimized conditions.



Scheme 9

Biological activities

Antioxidant activity

Recently, antioxidants been extensively discussed in relation to oxidative stress and radicals, cancer prophylaxis and therapy [37]. To study the free radical scavenging ability of the synthesized compounds (3g– 4l), the DPPH [diphenyl-(2,4,6-trinitrophenyl) iminoazanium] assay was used. The majority of compounds presented a good radical scavenging activity, though the compound 4j exhibited the strongest activity, even to the standard of ascorbic acid. Further studies are required to determine whether these main compounds could be a potential treatment for diabetes and hyperlipidaemia diseases.

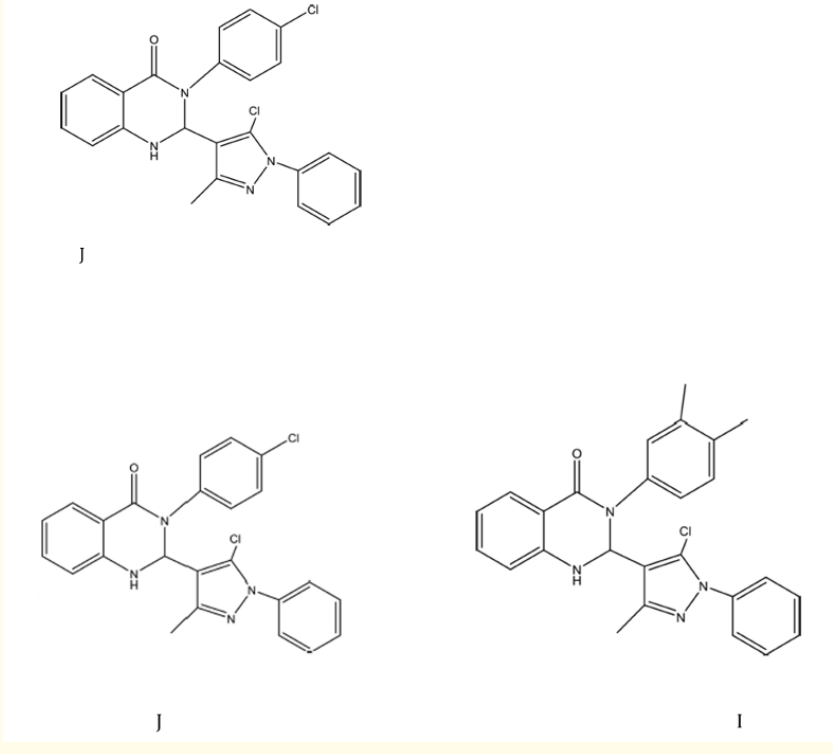


Figure 3

Figure 3j 2-(5-Chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)-3-(ptolyl)- 2,3-dihydroquinazolin-4(1H)-one.

The tested compounds, in particular, compounds 4j and 4l, were found to be uniquely reducing blood sugar levels [38].

Hatem A. Abuelizz., *et al*. [39] prepared a new series of quinazoline-4(3H)-ones and are evaluated for anticonvulsant activity. Out of twenty-four, compound Figure 4 proved to be the most active with a remarkable protection (100%) against PTZ induced convulsions and four times more potent activity than ethosuximide. benzyl substitution at position 3 has shown a strong anticonvulsant activity but with less seizure prevention compared to the butyl substitution.

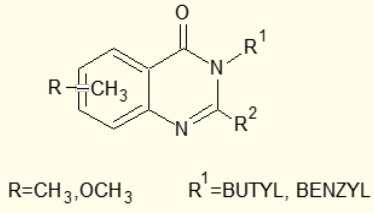


Figure 4: The structures of anticonvulsant and designed quinazolines.

Analgesic activity

Many quinazolines have been synthesized and evaluated for their analgesic and anti-inflammatory activities. 2-Phenyl quinazolinone. Figure 5 was synthesized by Alagarsamy., *et al*. in 2002 [40]. It was biologically evaluated as an analgesic agent.

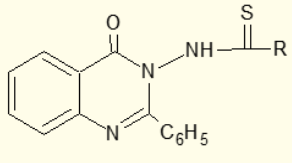


Figure 5

The modification of compound 1 to thiourea-substituted 2-methyl quinazolinone derivatives. Figure 6 produced more active compounds. The most active one was the compound which had the pyrrolidine ring at C-3 [41].

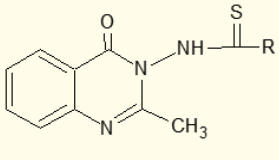


Figure 6

Alafeefy Ahmed M., *et al*. [42] were Synthesized some novel quinazoline derivatives and evaluated analgesic and anti-inflammatory All the new compounds were screened to evaluate their analgesic and anti-inflammatory activities and acute toxicity. Indomethacin was used as a reference standard. The analgesic activity was performed by the heat-induced nociception and the anti-inflammatory activity was evaluated by the formaldehyde-induced oedema techniques. It is worth to mention that the potent analgesic effect of compound. Figure 7 without any significant inhibition of inflammation and induction of S-shaped tail suggests that this compound seemed to be an opioid analgesic [43].

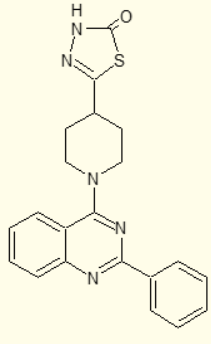


Figure 7

Anti-inflammatory activity

K.M. Amin., *et al*. [41] Synthesized, biologically evaluate and molecular docking of novel series of spiro [(2H,3H) quinazoline-2,10 - cyclohexan]-4(1H)- one derivatives as anti-inflammatory and analgesic agents. Three series of Spiro [(2H,3H) quinazoline-2,10 -cyclohexan]-4(1H)-one derivatives have been synthesized. Some of the novel quinazolinone derivatives II showed considerable potent anti-inflammatory and analgesic activity of in comparing to indomethacin and tramadol as reference drugs. Docking study into COX-2 has been made for derivatives of highest anti-inflammatory activity.

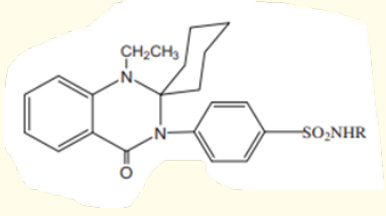


Figure 8

Alafeefy Ahmed M., *et al*. [42] were tested against formaldehyde induced inflammation, 6 compounds were considered devoid of activity, and 8 compounds showed weak anti-inflammatory activity. However, 13 compounds (6aej, 7b, 10, 12) showed significant inhibition, of which 6b and 6f were more potent than the reference drug and compound 7b was almost as active as indomethacin.

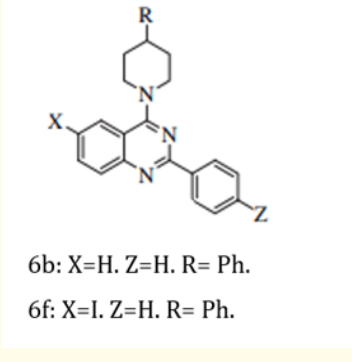


Figure 9

Fariba Peytam., *et al*. [43] was Designed, synthesized, and evaluate of novel substituted imidazole[1,2-*c*] quinazoline derivatives as potential *α*-glucosidase inhibitors with bioactivity and molecular docking insights. Among them, 2-(4-(((2,3-diphenylimidazo [1,2- c] quinazolin-5-yl) thio) methyl)-1H-1,2,3-triazol-1-yl)-N-(2-methoxyphenyl) acetamide (19e) showed good antidiabetic activity.

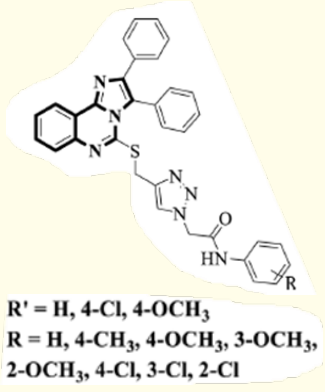


Figure 10

Anticancer agent

Shweta Mishra., *et al*. [44] was Designed, synthesized, molecular docking, and biological evaluation of quinazoline-tethered hydroxamic acid derivatives as HDAC inhibitors for anticancer activity. All three cancer cell lines were most sensitive to the N-hydroxyacrylamide derivatives as compared to Nhydroxybenzamides derivatives. In particular, compound 5a (0.39, 0.26, 0.41 μM respectively) and 5b (0.27, 0.57, 0.32 μM respectively) were found to be the most potent derivatives among all tested cell lines.

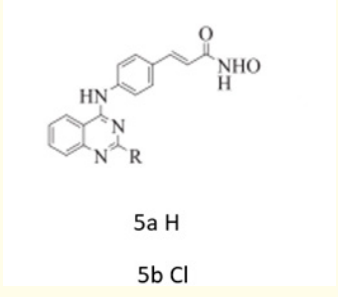


Figure 11

Alonso., *et al*. [45] describes the synthesis of 1,2,3,4-tetrahydroquinolinyl phosphine oxides, phosphanes and phosphine sulphides as well as that of quinolinyl phosphine oxides and phosphine sulfides. Among them most of the compounds showed excellent activity as topoisomerase I inhibitors. Human lung adenocarcinoma (A549), human embryonic kidney (HEK293), human ovarian carcinoma (SKOVO3) was also screened for the cytotoxic effect on cell lines. Against the lung cancer cell line compound figure 16 showed potent activity with IC50 value of 0.25±0.23 µm whereas compounds figure 12 and figure 13 showed better activity against lung cancer cell line with IC50 value of 0.08±0.01 µm and 0.03± 0.04 µm.

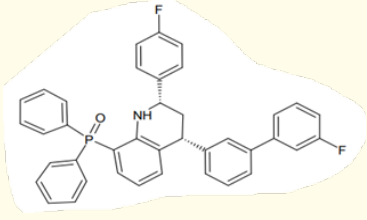


Figure 12

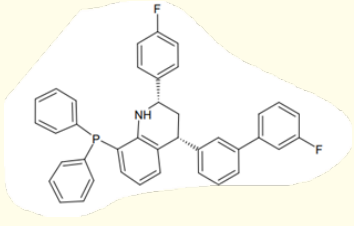


Figure 13

Yong-Feng Guan., *et al*. [46] was Designed, Synthesized, and evaluated their Anticancer Activity of Novel Quinoline-Chalcone Derivatives. Quinoline-chalcone derivatives were designed and synthesized, and explored their antiproliferative activity against MGC-803, HCT-116, and MCF-7 cells. Among these compounds, compound 14 exhibited a most excellent inhibitory potency against MGC-803, HCT-116, and MCF-7 cells with IC50 values of 1.38, 5.34, and 5.21 µM, respectively.

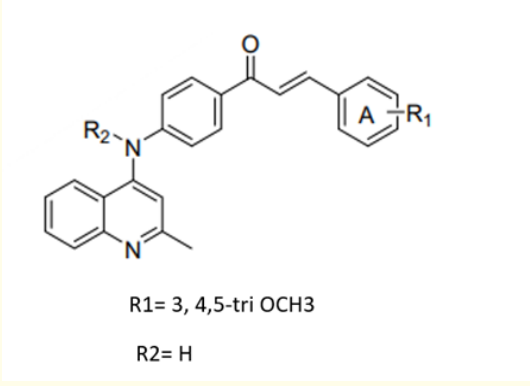


Figure 14

Zahra Emamgholipour., *et al*. [47] Synthesized and biologically evaluate in silico study of novel coumarin-quinazoline analogs as potential Anti-Angiogenesis agents. In cytotoxic tests conducted using the MTT assay, compound 13f exhibited significant anti-proliferative potency against HUVECs, with an IC50 value of 20.2 µM, compared to that of sorafenib (12.8 µM).

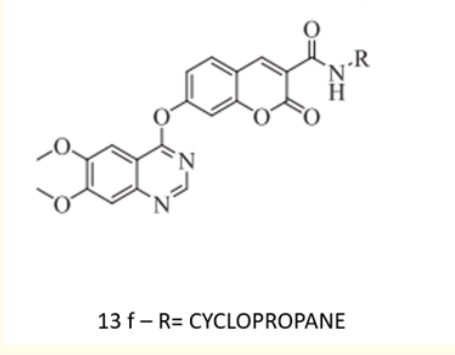
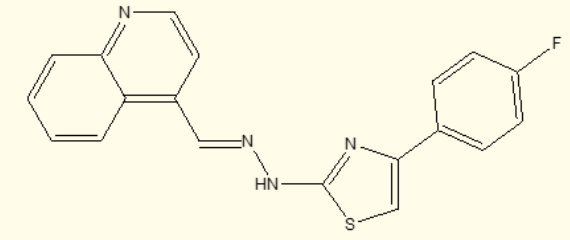


Figure 15

Antifugal agent

Mehlika Dilek Altintop., *et al*. [48] was synthesize new quinoline-based thiazolyl hydrazone derivatives and evaluate their anticandidal and anticancer effects. New thiazolyl hydrazone derivatives were evaluated for their anticandidal effects using disc diffusion method. 4-(4-Fluorophenyl)-2-(2-((quinolin-4-yl) methylene) hydrazinyl) thiazole (1) showed antifungal activity against Candida albicans and Candida krusei in the concentration of 1 mg/mL.

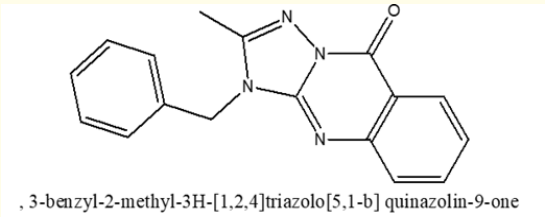


4-(4-Fluorophenyl)-2-(2-((quinolin-4-yl) methylene) hydrazinyl) thiazole

Figure 16

Antihypertensive agent

Veerachamy Alagarsamy., *et al*. [49] Synthesized and evaluate antihypertensive activity of novel 3-benzyl-2-substituted-3H-[1,2,4] triazolo[5,1-b] quinazolin-9-ones. A series of 3-benzyl-2-substituted-3H-[1,2,4] triazolo[5,1-b] quinazolin-9-ones have been synthesized by the cyclocondensation of 3-amino-2-benzyl-amino-3H-quinazolin-4-one with a variety of one-carbon donors. Among the series, 3-benzyl-2-methyl-3H-[1,2,4] triazolo[5,1-b] quinazolin-9-one (7b) was found to be the most active antihypertensive agent which is more potent than the reference standard prazocin.



, 3-benzyl-2-methyl-3H-[1,2,4]triazolo[5,1-b] quinazolin-9-one

7b

Figure 17

Caroon., *et al*. [50] synthesized the 2R*, llbS* and ZS*, llbS* diastereoisomers of the spiro [1,3,4,6,7,1 lb-hexahydro-2H-benzo[a] quinolizine-2,50 -oxazolidin-20 -one] system and evaluated for antihypertensive activity. Compound 54 was found to be most potent at 25 mg/kg. Percentage fall in blood pressure in 1 and 2 h was found to be 44 and 30% respectively.

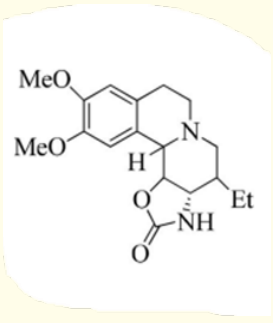


Figure 18

Conclusion

This review focuses on potent and diverse pharmacological activities of the derivatives of quinazoline moiety reported in the past years. It also delivers an outlook on recent developments of quinazoline derivatives having various biological activities like anticancer, antimalarial, antimicrobial, anticonvulsant and antidiabetic with lesser toxicity. Quinazoline is a structure of countless interest in the area of pharmaceutical chemistry, featuring various drugs, clinical candidates and bioactive molecules. The focus of this review was on the synthesis and potential biological activity of quinazoline derivatives. This review will provide significant benefit to scientists for the design and synthesis of quinazoline moiety-based drugs for the safe treatment of various fatal diseases in future.

Bibliography

1. X Yang. "Efficient copper-catalyzed synthesis of 4-aminoquinazoline and 2, 4-diaminoquinazoline derivatives". *Synletter* 1 (2010): 101-106.

2. Wang D and Gao F. "Quinazoline derivatives: Synthesis and bioactivities". *Chemistry Central Journal* 7 (2013): 1-15.

3. Chandregowda V., *et al*. "Synthesis and in vitro antitumor activities of novel 4-anilinoquinazoline derivatives". *European Journal of Medicinal Chemistry* 44 (2009): 3046-3055.

4. Al-Rashood ST., *et al*. "Synthesis, dihydrofolate reductase inhibition, antitumor testing, and molecular modeling study of some new 4 (3H)-quinazolinone analogs". *Bioorganic and Medicinal Chemistry* 14 (2006): 8608-8621.

5. Vasdev N., *et al*. "Synthesis of 6-acrylamido-4- (2-[18F] fluoroanilino) quinazoline: A prospective irreversible EGFR binding probe". *Journal of Labelled Compounds and Radiopharmaceuticals* 48 (2005): 109-115.

6. Wakeling AE., *et al*. "ZD1839 (Iressa): an orally active inhibitor of epidermal growth factor signaling with potential for cancer therapy". *Cancer Research* 62 (2002): 5749-5754.

7. Rohini R., *et al*. "Antimicrobial study of newly synthesized 6-substituted indolo[1,2-c] quinazolines". *European Journal of Medicinal Chemistry* 45 (2010): 1200-1205.

8. Antipenko L., *et al*. "Synthesis of new 2-thio- [1,2,4] triazolo[1,5-c] quinazoline derivatives and its antimicrobial activity". *Chemical and Pharmaceutical Bulletin* 57 (2009): 580-585.

9. Jatav V., *et al*. "Synthesis and antimicrobial activity of some new 3-[5- (4-substituted) phenyl-1,3,4-oxadiazole-2yl]-2-styrylquinazoline- 4 (3H)-ones". *Medicinal Chemistry Research* 17 (2008): 205-211.

10. Aly AA. "Synthesis of novel quinazoline derivatives as antimicrobial agents". *Chinese Journal of Chemistry* 21 (2003): 339-346.

11. Li H., *et al*. "Synthesis and bioactivity of 4-quinazoline oxime ethers". *Progress in Natural Science* 8 (1998): 359-365.

12. Chandrika PM., *et al*. "Synthesis leading to novel 2,4,6-trisubstituted quinazoline derivatives, their antibacterial and cytotoxic activity against THP-1, HL-60 and A375 cell lines". *Indian Journal of Chemistry* 48B (2009): 840-847.

13. Panneerselvam P., *et al*. "Anticonvulsant activity of Schiff bases of 3-amino-6,8-dibromo-2-phenylquinazolin- 4 (3H)-ones". *Indian Journal of Pharmaceutical Sciences* 72 (2010): 375-378.

14. Nandy P., *et al*. "Synthesis and antitubercular activity of Mannich bases of 2-methyl-3H-quinazolin-4-ones". *Indian Journal of Heterocyclic Chemistry* 15 (2006): 293-294.

15. Saravanan G., *et al*. "Synthesis and evaluation of antioxidant activities of novel quinazoline derivatives". *International Journal of Pharmaceutical Sciences and Research* 2 (2010): 83-86.

16. Lakhan R., *et al*. "Studies on 4 (3H)-quinazolinone derivatives as anti-malarials". *Journal of the Indian Chemical Society* 64 (1987): 316-318.

17. Hess HJ., *et al*. "Antihypertensive 2-amino-4 (3H)- quinazolinones". *Journal of Medicinal Chemistry* 11 (1968): 130-136.

18. Sasmal S., *et al*. "Design and optimization of quinazoline derivatives as melanin concentrating hormone receptor 1 (MCHR1) antagonists". *Bioorganic and Medicinal Chemistry Letters* 22 (2012): 3157-3162.

19. Alvarado M., *et al*. "Synthesis and biological evaluation of new quinazoline and cinnoline derivatives as potential atypical antipsychotics". *Chemistry and Biodiversity* 3 (2006): 106-117.

20. Malamas MS and Millen J. "Quinazolineacetic acids and related analogs as aldose reductase inhibitors". *Journal of Medicinal Chemistry* 34 (1991): 1492-1503.

21. Zayed MF and Hassan MH. "Synthesis and biological evaluation studies of novel quinazolinone derivatives as antibacterial and anti-inflammatory agents". *Saudi Pharmaceutical Journal* 22 (2014): 157-162.

22. El-Badry YA., *et al*. "Synthesis and evaluation of new polysubstituted quinazoline derivatives as potentialantimicrobial agents". *Der Pharma Chemica* 4 (2012): 1361-1370.

23. Dave RS., *et al*. "Synthesis, characterization and antimicrobial activity of new quinazolin- 4 (3H)-oneschiff base derivatives". *Journal of Chemical and Pharmaceutical Research* 4 (2012): 4864-4869.

24. Devi KA and Sriram MS. "Synthesis and antimicrobial activity of some quinazolinones derivatives". *International Journal of Drug* 4 (2012): 324-327.

25. Kyprianou N. "Doxazosin and terazosin suppress prostate growth by inducing apoptosis: clinical significance". *Journal of Urology* 169 (2003): 1520-1525.

26. Abida Parvez N., *et al*. "An updated review: newer quinazoline derivatives under clinical trial". *International Journal of Pharmaceutical and Biological Archive* 2 (2011): 1651-1657.

27. Moyer JD., *et al*. "Induction of apoptosis and cell cycle arrest by CP- 358,774, an inhibitor of epidermal growth factor receptor tyrosine kinase". *Cancer Research* 57 (1997): 4838-4848.

28. Asif M. "Chemical Characteristics, Synthetic Methods, and Biological Potential of Quinazoline and Quinazolinone Derivatives". *International Journal of Medicinal Chemistry* 2014 (2014): 1-27.

29. Zhang J., *et al*. "A Simple and Efficient Approach to the Synthesis of 2-Phenylquinazolines via sp3 C–H Functionalization". *Organic Letter* 12 (2010): 2841-2843.

30. G Chakraborty., *et al*. "Paul Dehydrogenative synthesis of quinolines, 2-aminoquinolines, and quinazolines using singlet diradical Ni (II)-catalysts". *Journal of Organic Chemistry* 84 (2019): 2626-2641.

31. Sarma R., *et al*. "Microwave-promoted efficient synthesis of dihydroquinazolines". *Green Chemistry* 13 (2011): 718-722.

32. DS Deshmukh., *et al*. "Molecular iodine catalysed benzylic sp3 C-H bond amination for the synthesis of 2-arylquinazolines from 2- aminobenzaldehydes, 2-aminobenzophenones and 2-aminobenzyl alcohols". *Synletter* 29 (2018): 979-985.

33. Bisht AS., *et al*. "Chemistry and activity of quinazoline moiety: A systematic review study". *International Journal of Pharmaceutical Chemistry and Analysis* 7 (2020): 61-65.

34. Molecular Operating Environment (MOE). Chemical Computing Group (2019).

35. Swiss Institute of Bioinformatics (SwissADME) (2022).

36. Alireza Barmak., *et al*. "Synthesis, Structural Studies, and α-Glucosidase Inhibitory, Antidiabetic, and Antioxidant Activities of 2,3-Dihydroquinazolin- 4 (1H) ones Derived from Pyrazol-4-carbaldehyde and Anilines". *ACS Omega* 4 (2019): 18087-18099.

37. Pisoschi A M and Negulescu GP. "Methods for Total Antioxidant Activity Determination: A Review". *Analytical and Bioanalytical Chemistry* 1 (2011): 106.

38. Alireza Barmak., *et al*. "Synthesis, Structural Studies, and α-Glucosidase Inhibitory, Antidiabetic, and Antioxidant Activities of 2,3-Dihydroquinazolin- 4 (1H)-ones Derived from Pyrazol-4-carbaldehyde and Anilines". *ACS Omega* 4 (2019): 18087-18099.

39. Hatem A Abuelizz., *et al*. "Molecular Docking and Anticonvulsant Activity of Newly Synthesized Quinazoline Derivatives". *Molecules* 22 (2017): 1094.

40. Alagarsamy V., *et al*. "Synthesis, analgesic, anti-inflammatory and anti-bacterial activities of some novel 2-methyl-3-substituted quinazolin-4 (3H)-ones". *Biological and Pharmaceutical Bulletin* 26 (2003): 1711-1714.

41. KM Amin., *et al*. "Synthesis, biological evaluation and molecular docking of novel series of spiro [(2H,3H) quinazoline-2,10 - cyclohexan]-4 (1H)- one derivatives as anti-inflammatory and analgesic agents". *European Journal of Medicinal Chemistry* 45 (2010): 2117-2131.

42. Ahmed M Alafeefy., *et al*. "Synthesis, analgesic and anti-inflammatory evaluation of some novel quinazoline derivatives". *European Journal of Medicinal Chemistry* 45 (2010): 4947e4952.

43. DL Bilbey., *et al*. *British Journal of Pharmacology and Chemotherapy* 4 (1960): 540-543.

44. Ahmed M Alafeefy., *et al*. "Synthesis, analgesic and anti-inflammatory evaluation of some novel quinazoline derivatives". *European Journal of Medicinal Chemistry* 45 (2010): 4947-4952.

45. Fariba Peytam., *et al*. "Design, synthesis, and evaluation of novel substituted imidazole[1,2-c] quinazoline derivatives as potential α-glucosidase inhibitors with bioactivity and molecular docking insights, scientific report nature. Com".

46. Shweta Mishra., *et al*. "Exploration of quinazoline-tethered hydroxamic acid derivatives as HDAC inhibitors for anticancer activity: Design, synthesis, molecular docking, and biological evaluation Results in Chemistry". 7 (2024): 101253.

47. Alonso C., *et al*. "Novel topoisomerase I inhibitors. Syntheses and biological evaluation of phosphorus substituted quinoline derivates with antiproliferative activity". *European Journal of Medicinal Chemistry* 149 (2018): 225-237.

48. Yong-Feng Guan., *et al*. "Design, Synthesis, and Anticancer Activity Studies of Novel Quinoline-Chalcone Derivatives Yong-Feng Guan". *Molecules* 26 (2021): 4899.

49. Zahra Emamgholipour., *et al*. "Synthesis, biological evaluation, and in silico study of novel coumarin-quinazoline analogs as potential Anti-Angiogenesis agents". *Results in Chemistry* 11 (2024): 101819.

50. Ali Erguc Mehlika Dilek Altintop., *et al*. "Synthesis and Biological Evaluation of New Quinoline-Based Thiazolyl Hydrazone Derivatives as Potent Antifungal and Anticancer Agents". *Letters in Drug Design and Discovery* 15.2 (2018): 193-202.

51. Veerachamy Alagarsamya and Urvishbhai S Pathak. "Synthesis and antihypertensive activity of novel 3-benzyl-2-substituted-3H- [1,2,4] triazolo[5,1-b] quinazolin-9-ones". *Bioorganic and Medicinal Chemistry* 15 (2007): 3457-3462

52. Caroon JM., *et al*. "Synthesis and Antihypertensive Activity of a Series of Spiro [1,3,4,6,7,11b-hexahydro-2H-benzo quinolizine2,50 -oxazolidin-20 -oriels". *Journal of Medicinal Chemistry* 26 (1983): 1426-1433.