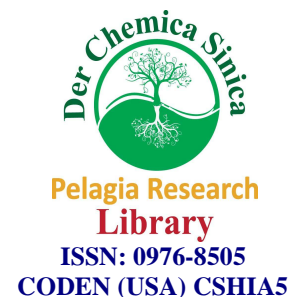




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Quinazolin-4-one: A highly important heterocycle with diverse biological activities: A review

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ABSTRACT

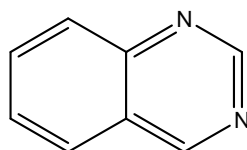
Quinazolin-4-one and their derivatives have been studied extensively for various biological activities such as anti-inflammatory, antimicrobial, anticancer, anticonvulsant and anti-HIV activity etc. The purpose of this review was to collate literature work reported by researchers on quinazoline and specifically quinazolin-4-one for their various pharmacological activities. This review might be helpful in the development of these novel lead molecules to potential drug candidates for future prospect.

Keywords: Quinazolin-4-one, Anti HIV, Anti cancer, novel lead molecules.

INTRODUCTION

Heterocyclic chemistry comprises at least half of all organic chemistry research worldwide. In particular, heterocyclic structures form the basis of many pharmaceutical, agrochemical and veterinary products. Quinazoline¹⁻⁵(Fig.1) are classes of fused heterocycles that are of considerable interest because of the diverse range of their biological activities such as, anti-microbial, anti-cancer, anticonvulsant, anti-tubercular, etc.

Quinazolin is a heterocyclic compound consists of two fused six membered simple aromatic rings, a benzene ring and a pyrimidine ring.

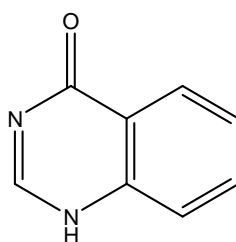


Quinazolin

Fig.1

According to recent data, quinazolin nucleus has attracted the attention of medicinal chemists due to its well known anticancer activity, and many substituted quinazolin derivatives have recently earned great interest in chemotherapy as antitumor drugs.⁶

Pharmacologically quinazolin particularly quinazolin-4-one (Fig.2) or quinazolinone are among the most important classes of heterocyclic compounds. Quinazolin-4-one is synthesized when the keto group is introduced in the pyrimidine ring of quinazolin. These compounds possess versatile type of biological activities; some of these are well known for their anticancer⁷⁻⁸, antitubercular⁹, antibacterial¹⁰, antifungal¹¹, anti-HIV¹², anthelmintic¹³, anti-inflammatory¹⁴ and antihypertensive activities¹⁵.



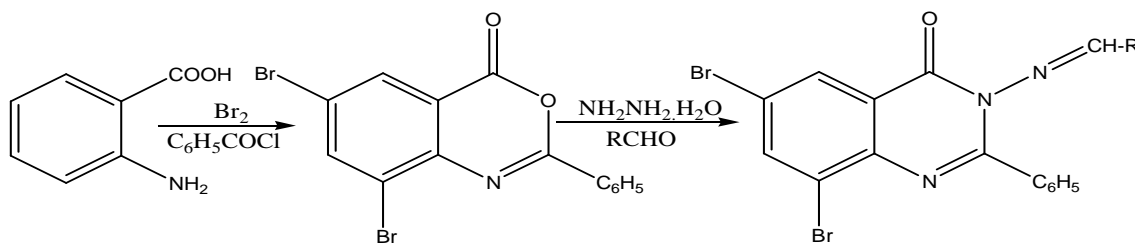
quinazolin-4-one

Fig.2

CHEMISTRY

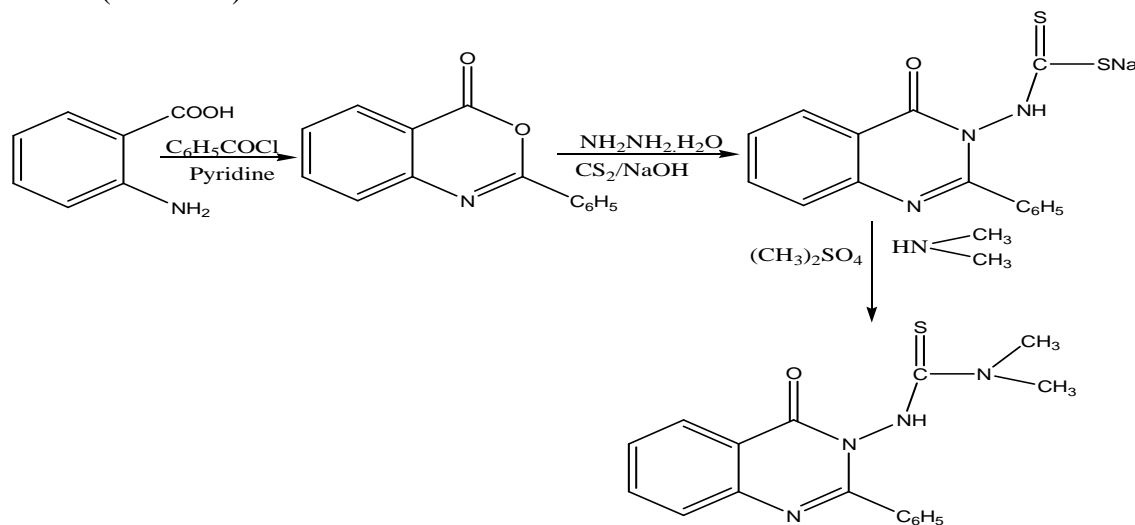
Various methods have been proposed by various researchers for the synthesis of quinazolin-4-ones as mentioned below. Anthranilic acid is the key reagent for the synthesis of quinazolin-4-ones.

Panneerselvam P. *et al.* (2009) synthesized some Schiff bases of 3-amino-6, 8-dibromo-2 phenylquinazolin-4(3H)-ones.¹⁶ (Scheme 1)

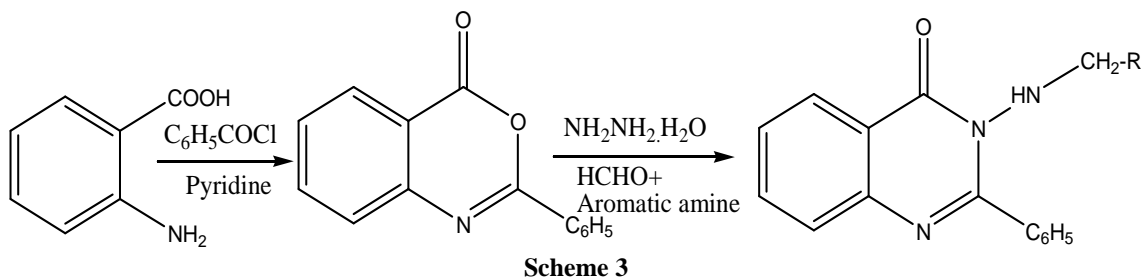


Scheme 1

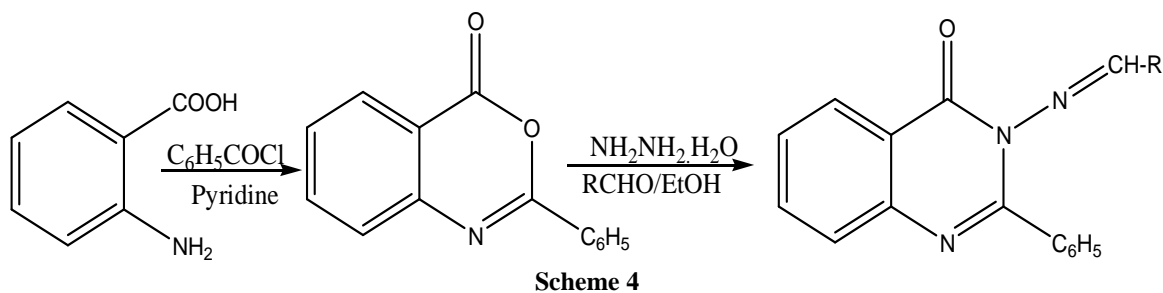
Alagarsamy V. *et al.* (2002) synthesized some novel 2-phenyl-3-substituted quinazolin-4(3*H*) Ones.¹⁷ (Scheme 2)



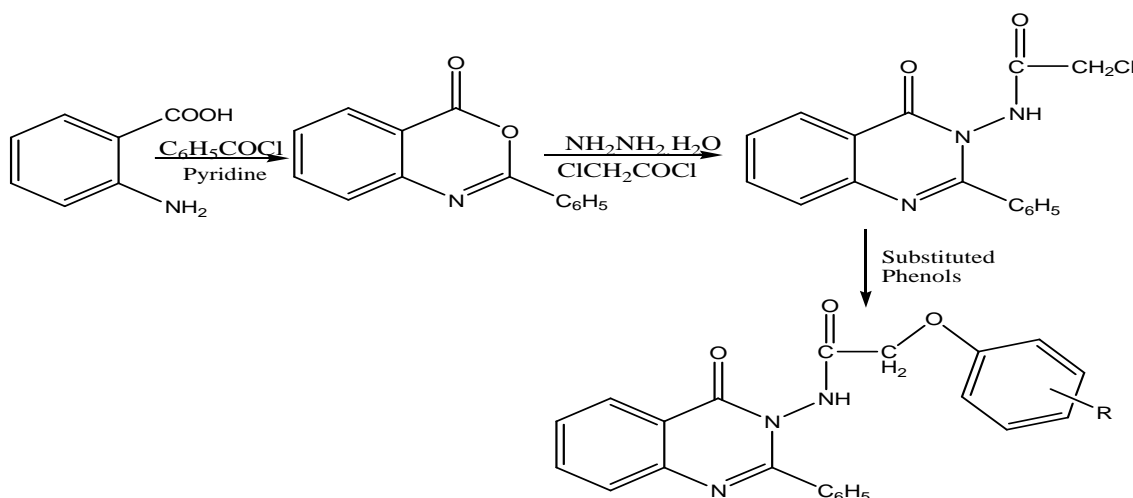
Saravanan S. *et al.* (2010) synthesized some 2-phenyl 3-substituted quinazolin-4(3*H*)-ones derivatives.¹⁸ (Scheme 3)



Mariappan G. *et al.* (2011) synthesized quinazolinone fused Schiff bases.¹⁹ (Scheme 4)

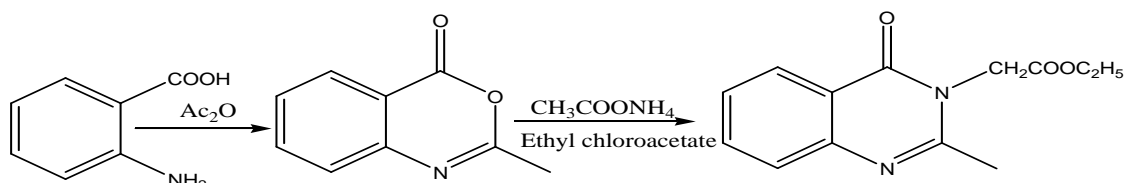


Kohli Deepti *et al.* (2009) synthesized some novel quinazolinone derivatives.²⁰ (Scheme 5)



Scheme 5

Kotgire S.Sandip *et al.* (2010) Synthesis of ethyl 2-(2-methyl-4-oxoquinazolin-3(4H)-yl) acetate as important analog and intermediate of 2,3 disubstituted quinazolinones.²¹ (Scheme 6)



Scheme 6

PHARMACOLOGICAL ACTIVITIES

1. Analgesic and anti-inflammatory agents

Some novel quinazolin-4-one derivatives show promising analgesic and anti-inflammatory activities. The novel derivatives of quinazolines mentioned might be beneficial in terms of biological activity for which further studies can be done to confirm it as a potential drug candidate.

Alagarsamy V.*et al.* (2002) synthesized some novel 2-phenyl-3-substituted quinazolin-4(3H) ones (Fig.3) derivatives and evaluated them for analgesic and anti-inflammatory activity compared with Diclofenac sodium as standard drug.¹⁷

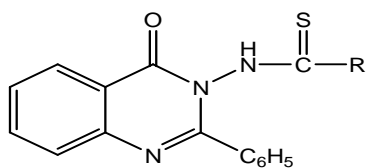


Fig.3

| S. No. | Substitution(R) | Activities Reported |
|--------|-------------------|-------------------------------------------|
| 3a. | N-CH ₃ | Analgesic and anti- inflammatory activity |
| 3b. | | Analgesic and anti- inflammatory activity |
| 3c. | | Analgesic and anti- inflammatory activity |
| 3d. | | Analgesic activity |
| 3e. | | Analgesic activity |
| 3f. | | Analgesic activity |
| 3g. | | Analgesic activity |
| 3h. | | Analgesic activity |
| 3i. | | Analgesic activity |
| 3j. | | Analgesic activity |
| 3k. | | Analgesic activity |

Mariappan G.*et al.* (2011) synthesized quinazolinone fused Schiff bases (Fig.4) and evaluated them for anti-inflammatory activity.¹⁹

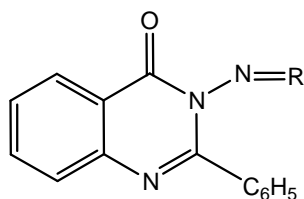


Fig.4

| S. No. | Substitution(R) | Activities Reported |
|--------|---------------------------------|----------------------------|
| 4a. | 2-nitrobenzaldehyde | Anti-inflammatory activity |
| 4b. | Cinnamaldehyde | Anti-inflammatory activity |
| 4c. | Acetaldehyde | Anti-inflammatory activity |
| 4d. | Furfuraldehyde | Anti-inflammatory activity |
| 4e. | 2-chlorobenzaldehyde | Anti-inflammatory activity |
| 4f. | 3-methoxy-4-hydroxybenzaldehyde | Anti-inflammatory activity |

B.A. Rather *et al.* (2010) also worked on quinazolin-4(3H)-ones (Fig.5) to produce different compounds of varied potency when compared with the standard aspirin and indomethacin²².

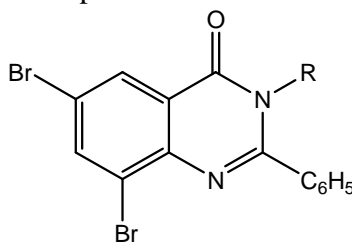
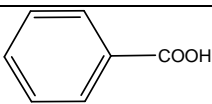
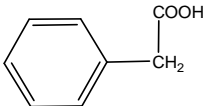


Fig.5

| S. No. | Substitution(R) | Activities Reported |
|--------|-------------------------------------------------------------------------------------|------------------------------------------|
| 5a |  | Analgesic and anti-inflammatory activity |
| 5b |  | Analgesic and anti-inflammatory activity |

2. Anti-microbial agents

Anti-microbials cover large spectrum biological activities like anti bacterial, anti fungal, anti viral, anti leishmanial, antiprotozoal, antiplasmodial etc. Several derivatives of quinazolins possess potential anti-microbial activities.

Panneerselvam P. *et al.* (2009) synthesized some Schiff bases of 3-amino-6, 8-dibromo-2-phenylquinazolin-4(3H)-ones (Fig.6) and these compounds are screened as antimicrobial agents.¹⁶

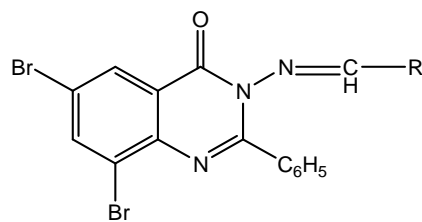
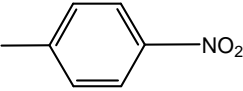
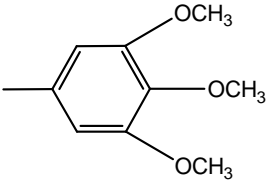
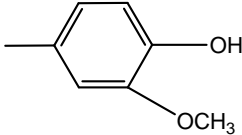
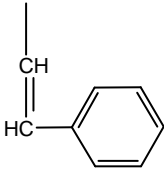


Fig.6

| S. No. | Substitution(R) | Activities Reported |
|--------|-----------------|---------------------------------------|
| 6a. | | Antifungal and antibacterial activity |
| 6b. | | Antifungal and antibacterial activity |
| 6c. | | Antifungal and antibacterial activity |
| 6d. | | Antifungal and antibacterial activity |
| 6e. | | Antifungal and antibacterial activity |
| 6f. | | Antifungal and antibacterial activity |
| 6g. | | Antifungal and antibacterial activity |
| 6h. | | Antifungal and |

| | | |
|-----|------------------------------------------------------------------------------------|---------------------------------------|
| | | antibacterial activity |
| 6i. |  | Antifungal and antibacterial activity |
| 6j. |  | Antifungal and antibacterial activity |
| 6k. |  | Antifungal and antibacterial activity |
| 6l. |  | Antifungal and antibacterial activity |

Raghavendra M.*et al.* (2007) synthesized some novel substituted 2-Imidazolyl-*N*-(4-oxo-quinazolin-3(4*H*)-yl)-acetamides derivatives (Fig.7) and evaluated the Antimicrobial activities.²³

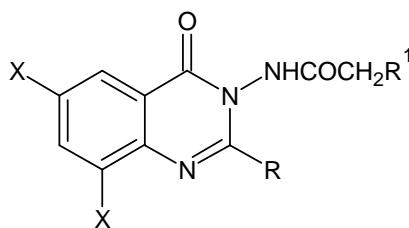


Fig.7

| S. No. | Substitutions | | | Activities Reported |
|--------|---------------|-------------------------------|--------------------------|-------------------------|
| | X | R | R ¹ | |
| 7a. | H | C ₆ H ₅ | Imidazolyl | Antibacterial activity |
| 7b. | H | C ₆ H ₅ | 2-Methyl Imidazolyl | Antitubercular activity |
| 7c. | H | C ₆ H ₅ | 2-Methyl benziimidazolyl | Antibacterial activity |
| 7d. | H | C ₆ H ₅ | Benziimidazolyl | Antibacterial activity |
| 7e. | Br | C ₆ H ₅ | Imidazolyl | Antibacterial activity |
| 7f. | Br | C ₆ H ₅ | 2-Methyl Imidazolyl | Antitubercular activity |
| 7g. | Br | C ₆ H ₅ | 2-Methyl benziimidazolyl | Antibacterial activity |
| 7h. | Br | C ₆ H ₅ | Benziimidazolyl | Antibacterial activity |
| 7i. | Br | CH ₃ | Imidazolyl | Antibacterial activity |
| 7j. | Br | CH ₃ | 2-Methyl Imidazolyl | Antibacterial activity |

| | | | | |
|-----|----|-------------------------------|--------------------------|-------------------------|
| 7k. | Br | CH ₃ | 2-Methyl benziimidazolyl | Antibacterial activity |
| 7l. | Br | CH ₃ | Benziimidazolyl | Antibacterial activity |
| 7m. | Br | C ₃ H ₇ | Imidazolyl | Antibacterial activity |
| 7o. | Br | C ₃ H ₇ | 2-Methyl Imidazolyl | Antibacterial activity |
| 7p. | Br | C ₃ H ₇ | 2-Methyl benziimidazolyl | Antitubercular activity |
| 7q. | Br | C ₃ H ₇ | Benziimidazolyl | Antibacterial activity |

Nanda A.K *et al.* (2007) synthesized some 3-(arylideneamino)-2-phenylquinazoline-4(3H)-ones derivatives (Fig.8) and screened them for antibacterial activity.²⁴

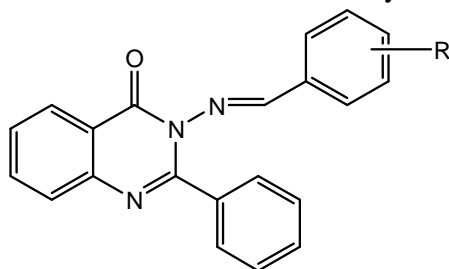


Fig.8

| S. No. | Substitution(R) | Activities Reported |
|--------|--------------------------|------------------------|
| 8a. | 2' '-OH | Antibacterial activity |
| 8b. | 4' '-OCH ₃ | Antibacterial activity |
| 8c. | 4' '-F | Antibacterial activity |
| 8d. | 4' '-N(CH ₃) | Antibacterial activity |
| 8e. | 4' '-Cl | Antibacterial activity |
| 8f. | 3' '-OCH ₃ | Antibacterial activity |
| 8g. | 4' '-OH | Antibacterial activity |
| 8h. | 4' '-OCH ₃ | Antibacterial activity |
| 8i. | 4' '-OH | Antibacterial activity |
| 8j. | 4' '-NO ₂ | Antibacterial activity |
| 8k. | H | Antibacterial activity |

Ilango K *et al.* (2010) synthesize newer quinazolin-4- (3H)-one clubbed isatin derivatives (Fig.9) as potent antimicrobial agents.²⁵

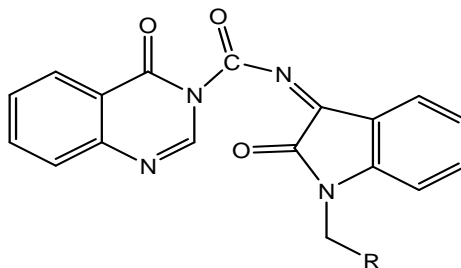
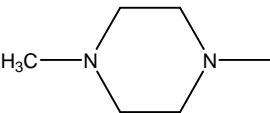
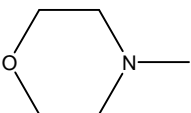
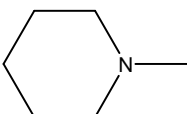
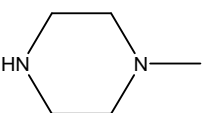
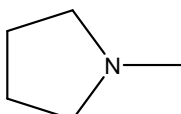


Fig.9

| S. No. | Substitution(R) | Activities Reported |
|--------|-------------------------------------------------------------------------------------|---------------------------------------|
| 9a. |  | Antifungal and antibacterial activity |
| 9b. |  | Antifungal and antibacterial activity |
| 9c. |  | Antifungal and antibacterial activity |
| 9d. |  | Antifungal and antibacterial activity |
| 9e. |  | Antifungal and antibacterial activity |
| 9f. | $(C_2H_5)_2N$ — | Antifungal and antibacterial activity |

Ramarao *et.al* (2010) worked on several new quinazolinone formazans (Fig.10) which were evaluated for their anti microbial and antihelminthic property which were comparable to ciprofloxacin, fluconazole, albendazole and piperazine citrate respectively, among whom the following were found to be potent.²⁶

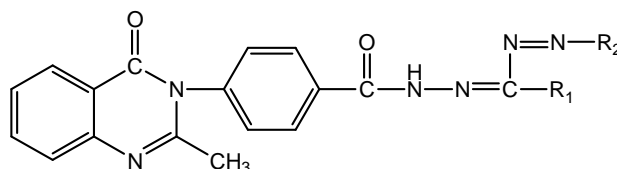


Fig.10

| S. No. | Substitution | | Activities Reported |
|--------|----------------------------------------------------------------|----------------------------------|---------------------------------------|
| | R ₁ | R ₂ | |
| 10a. | C ₆ H ₄ NO ₂ | C ₆ H ₃ Cl | Antimicrobial and antifungal activity |
| 10b. | C ₆ H ₆ N(CH ₃) ₂ | C ₆ H ₄ Cl | Antimicrobial and antifungal activity |
| 10b. | C ₆ H ₃ (OH)(OCH ₃) | C ₆ H ₃ Cl | Antimicrobial and antifungal activity |

3. Anticonvulsant agents

Some quinazolinone derivatives shows promising anticonvulsant activities. For the future prospect quinazolinone can be the suitable candidate for the treatment of convulsions.

Kumar A. *et al.* (2010) synthesis, characterization and biological activity of various thiadiazolopyridinyl (Fig.11) /indolyloxazolyl (Fig.12) quinazolinone-4-ones.²⁷

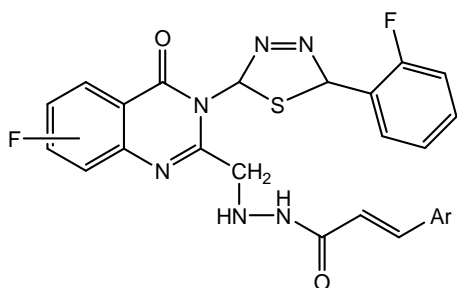


Fig.11

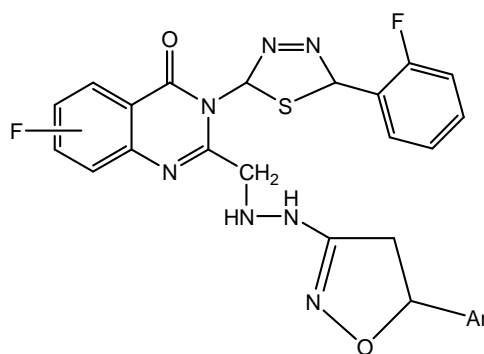
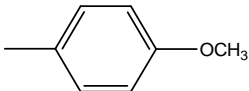
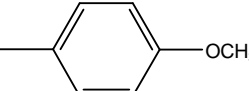
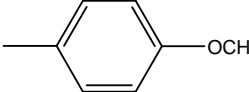
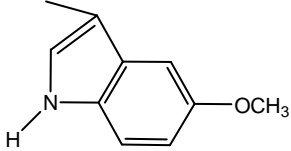
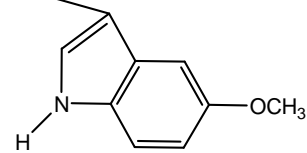
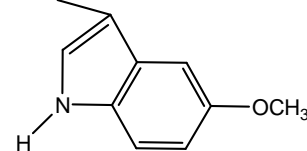
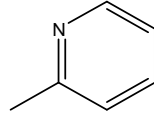
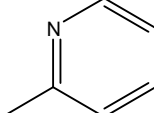
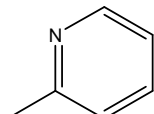
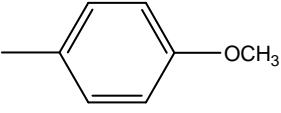


Fig.12

| S. No. | Substitutions | | Activities Reported |
|--------|----------------|----------------|-------------------------------------------|
| | R ₁ | R ₂ | |
| 11a. | H | | Anticonvulsant and antipsychotic Activity |
| 11b. | 6-Br | | Anticonvulsant and antipsychotic activity |
| 11c. | 6,8-Br | | Anticonvulsant and antipsychotic activity |

| | | | |
|------|--------|-------------------------------------------------------------------------------------|----------------------------------------|
| 11d. | H |  | Anticonvsant and antipsycotic activity |
| 11e. | 6-Br |  | Anticonvsant and antipsycotic activity |
| 11f. | 6,8-Br |  | Anticonvsant and antipsycotic activity |
| 11g. | H |  | Anticonvsant and antipsycotic activity |
| 11h. | 6-Br |  | Anticonvsant and antipsycotic activity |
| 11i. | 6,8-Br |  | Anticonvsant and antipsycotic activity |
| 12a. | H |  | Anticonvsant and antipsycotic Activity |
| 12b. | 6-Br |  | Anticonvsant and antipsycotic activity |
| 12c. | 6,8-Br |  | Anticonvsant and antipsycotic activity |
| 12d. | H |  | Anticonvsant and antipsycotic activity |

| | | | |
|------|--------|--|-------------------------------------------|
| 12e. | 6-Br | | Anticonvulsant and antipsychotic activity |
| 12f. | 6,8-Br | | Anticonvulsant and antipsychotic activity |
| 12g. | H | | Anticonvulsant and antipsychotic activity |
| 12h. | 6-Br | | Anticonvulsant and antipsychotic activity |
| 12i. | 6,8-Br | | Anticonvulsant and antipsychotic activity |

Ghany abdel *et al.* (2009) synthesized some new derivatives of 3*H*-quinazolin-4-one (Fig.13) through condensation reaction of their potassium salts with methyl, ethyl and phenyl isocyanate and synthesized compounds showed promising anticonvulsant activity.²⁸

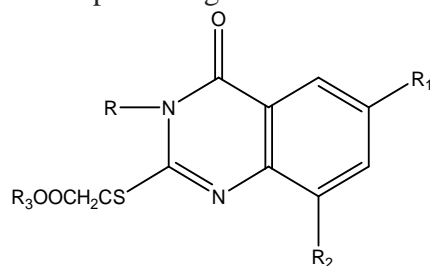


Fig.13

| S. No. | Substitutions | | | | Activity Reported |
|--------|-----------------|----------------|----------------|----------------|-------------------------|
| | R | R ₁ | R ₂ | R ₃ | |
| 13. | CH ₃ | H | H | Phenyl | Anticonvulsant activity |

Georgey Hanan *et al.* (2008) synthesized quinazolin-4-(3*H*)-one derivatives (Fig.14) as Anticonvulsant activity.²⁹

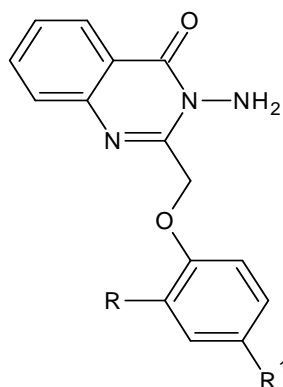


Fig.14

| S. No. | Substitutions | | Activity Reported |
|--------|----------------|----------------|-------------------------|
| | R ₁ | R ₂ | |
| 14. | H | Cl | Anticonvulsant activity |

Vaidya A. Niteen *et al.* (1983) synthesized 3,4-Dihydro-4-oxoquinazolin derivative (Fig.15,16) by the use of 2-amino-3-cyano-4,5-dimethyl furan and methyl acrylate and evaluated the anticonvulsant activity of synthesized compound.³⁰

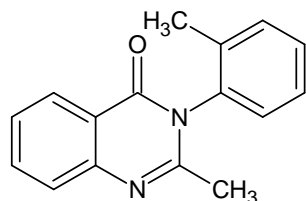


Fig.15

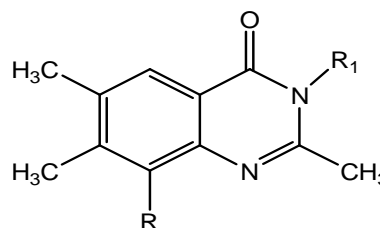


Fig.16

| S. No. | Substitutions | | Activity Reported |
|--------|---------------|---------------------------------|-------------------------|
| | R | R ₁ | |
| 16. | COOH | p-C ₆ H ₄ | Anticonvulsant activity |

4. Anti HIV agents

Quinazolin-4-(3H)-one is a versatile lead molecule for the design of potential bioactive agents. Alagarsamy *et al.* (2000)³¹ Shah *et al.* (1995)³² and Desai *et al.* (1998)³³, reported anti-hiv activity of 2-phenyl-3-substituted quinazolin-4-(3H)-ones. The literatures also reinforces that the 2-phenyl-3-substituted quinazolin-4-(3H)-ones. A large number of quinazolines have been synthesized and studied for wide range of anti-viral activity but the anti-viral activities of quinazolines against viruses has not been well explored.

Saravanan S. *et al.* (2010) synthesis, antiviral and studies of some 2-phenyl 3-substituted quinazolin-4(3H)ones (Fig.17).¹⁸

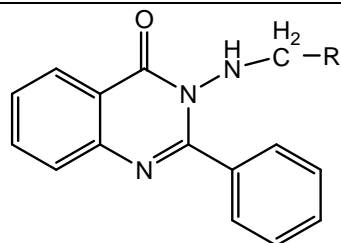
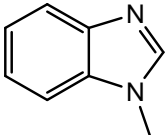
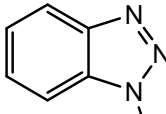
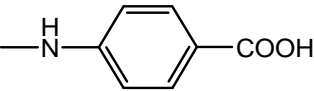
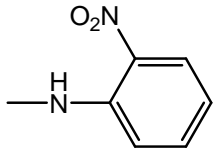


Fig.17

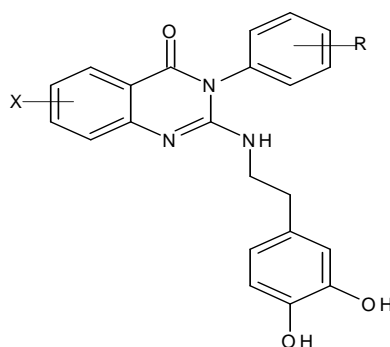
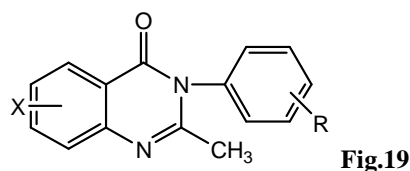
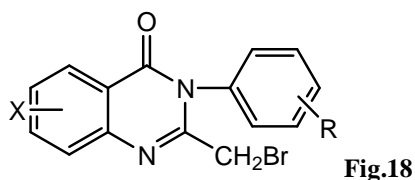
| S. No. | Substitution(R) | Activities Reported |
|--------|-----------------|---------------------|
| 17a. | | Anti HIV |
| 17b. | | Anti HIV |
| 17c. | | Anti HIV |
| 17d. | | Anti HIV |
| 17e. | | Anti HIV |
| 17f. | | Anti HIV |
| 17g. | | Anti HIV |

| | | |
|------|-----------------------------------------------------------------------------------|----------|
| 17h. |  | Anti HIV |
| 17i. |  | Anti HIV |
| 17j. |  | Anti HIV |
| 17k. |  | Anti HIV |

5. Antiparkinson agents

Parkinsonism is caused due to deficiency of dopamine. After the attachment of dopamine with some quinazolin, these derivative shows promising antiparkinson activity.

Kumar Sunil *et al.* (2010) synthesized a series of 3-substituted phenyl 2- (3,4-dihydroxy phenyl ethyl amino)-6-substituted quinazolin-4-(3H) ones (Fig.18,19,20) by the reaction of 3-Substituted phenyl -2-methylbromo-6-substituted quinazolin-4-(3H) ones with dopamine (3,4 dihydroxy phenyl ethyl amine) and has shown most potent antiparkinsonian activity.³⁴



| S. No. | Substitutions | | Activity Reported |
|--------|---------------|----------------------------------------|---------------------------|
| | X | R | |
| 18a. | H | H | Antiparkinsonian activity |
| 18b. | H | 2-Cl | Antiparkinsonian activity |
| 18c. | H | 4-OCH ₃ , 2-CH ₃ | Antiparkinsonian activity |
| 18d. | H | 2-OCH ₃ | Antiparkinsonian activity |
| 18e. | Br | H | Antiparkinsonian activity |
| 18f. | Br | 2-Cl | Antiparkinsonian activity |
| 18g. | Br | 4-OCH ₃ , 2-CH ₃ | Antiparkinsonian activity |
| 18h. | Br | 2-OCH ₃ | Antiparkinsonian activity |
| 19a. | H | H | Antiparkinsonian activity |
| 18b. | H | 2-Cl | Antiparkinsonian activity |
| 19c. | H | 4-OCH ₃ , 2-CH ₃ | Antiparkinsonian activity |
| 18d. | H | 2-OCH ₃ | Antiparkinsonian activity |
| 19e. | Br | H | Antiparkinsonian activity |
| 19f. | Br | 2-Cl | Antiparkinsonian activity |
| 19g. | Br | 4-OCH ₃ , 2-CH ₃ | Antiparkinsonian activity |
| 19h. | Br | 2-OCH ₃ | Antiparkinsonian activity |
| 20a. | H | H | Antiparkinsonian activity |
| 20b. | H | 2-Cl | Antiparkinsonian activity |
| 20c. | H | 4-OCH ₃ , 2-CH ₃ | Antiparkinsonian activity |
| 20d. | H | 2-OCH ₃ | Antiparkinsonian activity |
| 20e. | Br | H | Antiparkinsonian activity |
| 20f. | Br | 2-Cl | Antiparkinsonian activity |
| 20g. | Br | 4-OCH ₃ , 2-CH ₃ | Antiparkinsonian activity |
| 20h. | Br | 2-OCH ₃ | Antiparkinsonian activity |

6. Antitubercular agents

There are no promising quinazolines marketed presently in the category of tuberculosis. But several novel molecules have been synthesized in the past which showed promising results but unfortunately could not make it up to the marketing stage.

Rajasekaran S *et al.* (2010) synthesize some 2-phenyl-3-substituted quinazolin-4(3*H*)-ones (Fig.21) and evaluate the antitubercular activities.³⁴

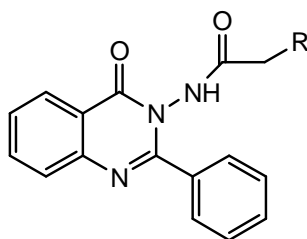
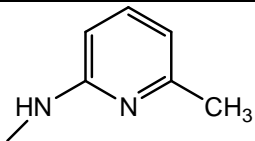
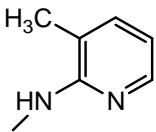
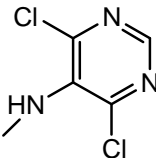
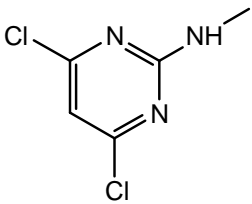
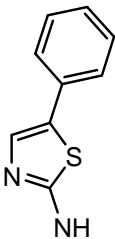
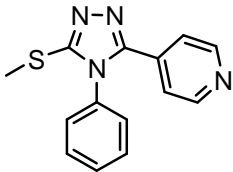
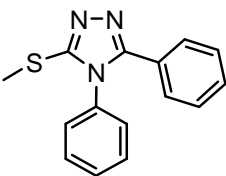


Fig.21

| S. No. | Substitution(R) | Activities Reported |
|--------|-------------------------------------------------------------------------------------|---------------------|
| 21a. |  | Antitubercular and |

| | | |
|------|--------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|
| 21b. |  <chem>CN1C=CC=C(C)N1</chem> | Antioxidant activity |
| 21c. |  <chem>CN1C=NC(Cl)=C(Cl)N1</chem> | Antitubercular and Antioxidant activity |
| 22d. |  <chem>CN1C=NC(Cl)=C(Cl)N1</chem> | Antitubercular and Antioxidant activity |
| 22e. |  <chem>Nc1nc(s1)C2=CC=CC=C2</chem> | Antitubercular and Antioxidant activity |
| 22f. |  <chem>C1=CC=C(C=C1)N2C(=N1C=CC=C1)S2C3=CC=C(C=C3)N</chem> | Antitubercular and Antioxidant activity |
| 22g. |  <chem>C1=CC=C(C=C1)N2C(=N1C=CC=C1)S2C3=CC=CC=C3</chem> | Antitubercular and Antioxidant activity |

Pattan R.S *et al.* (2006) synthesis of N-3(4-(4-chlorophenyl thiazol-2-yl)-(2-(amino) methyl) quinazolin4(3H)-one (Fig.22) and their derivative for antitubercular activity.³⁵

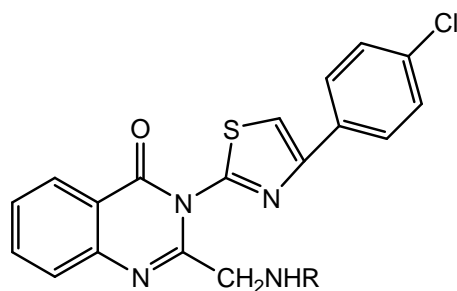
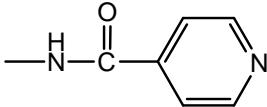
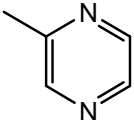
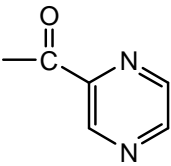
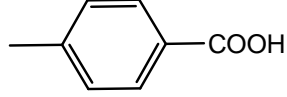
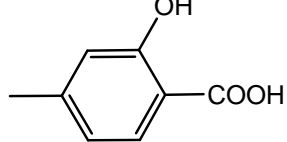


Fig.22

| S. No. | Substitution(R) | Activity Reported |
|--------|-------------------------------------------------------------------------------------|-------------------------|
| 22a. | C ₆ H ₄ Cl | Antitubercular activity |
| 22b. | C ₆ H ₄ F | Antitubercular activity |
| 22c. | C ₆ H ₄ NO ₂ | Antitubercular activity |
| 22d. | C ₆ H ₄ CH ₃ | Antitubercular activity |
| 22e. | C ₆ H ₄ OCH ₃ | Antitubercular activity |
| 22f. |  | Antitubercular activity |
| 22g. |  | Antitubercular activity |
| 22h. |  | Antitubercular activity |
| 22i. |  | Antitubercular activity |
| 22j. |  | Antitubercular activity |

7. Anti cancer agents

Quinazolines occupy a promising section in the anti-cancer activity because of their specificity. There are so many researcher synthesize the quinazolin derivatives as anti cancer drug.

Conconi *et al.* (2010) synthesized several dioxolane, dioxane (Fig.23), and dioxepine quinazoline derivatives and stated that size of the fused dioxygenated ring was crucial for the biological activity, the dioxane derivatives being the most promising class of this series. Derivatives were able to counteract EGF-induced EGFR phosphorylation and showed better or at least comparable

potency with respect to PD153035 of which the following compound was promising.³⁶

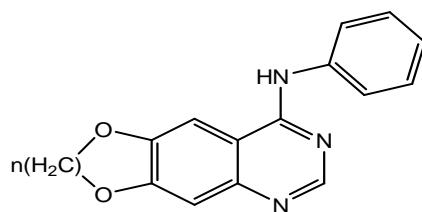


Fig.23

Sirisoma *et al.* (2010) synthesized several N-methyl-4-(4-methoxyanilino) quinazolines (Fig.24) and stated that substitution at the 5-, 6-, 7-positions of the quinazoline and replacement of the quinazoline by other nitrogen-containing heterocycles. Replacement of the quinazoline ring with a quinoline, a benzo[d][1,2,3]triazine, or an isoquinoline ring showed that the nitrogen at the 1-position is important for activity, while the carbon at the 2-position can be replaced by a nitrogen and then nitrogen at the 3-position can be replaced by a carbon. The following compounds were found to be potent when compared with standard Azixa.³⁷

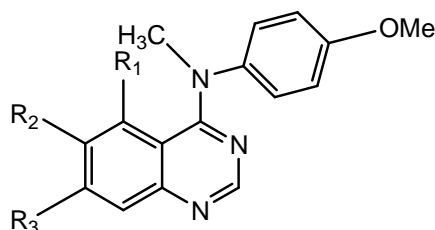


Fig.24

| S. No. | Substitutions | | | Activity Reported |
|--------|----------------|-----------------|----------------|----------------------|
| | R ₁ | R ₂ | R ₃ | |
| 24a. | H | NH ₂ | H | Anti cancer activity |
| 24a. | H | NO ₂ | H | Anti cancer activity |

8. Anti-Histaminic agents:

In the recent days lot of research is being done in the category of histaminic antagonists with relatively less sedation effect than existing drugs. Some quinazoline possess good antihistaminic properties.

Alagaraswamy *et al.* synthesized several 4-(3-ethylphenyl)-1-substituted-4H [1,2,4] triazolo [4,3-*a*]quinazolin-5-ones (2009)³⁸, 4-(4-ethylphenyl)-1-substituted-substituted-4H [1,2,4] triazolo [4,3-*a*] quinazolin-5-ones(2008)³⁹ and 1-substituted-4-cyclohexyl-4H-[1,2,4] triazolo [4,3-*a*] quinazolin-5-ones(2007)⁴⁰.

It was found that by varying substitution over the first position of the triazolo quinazoline ring there was variation in the biological activity. The presence of methyl group showed better activity than the unsubstituted compound. With increased lipophilicity the activity remained but further

increase in lipophilicity led to a decrease in activity. Replacement of the methyl group by other groups decreased the activity. The anti-histaminic potential was tested *in vivo* by comparing with Chlorpheniramine maleate in which the following compound showed promising anti histaminic activity with less sedation.

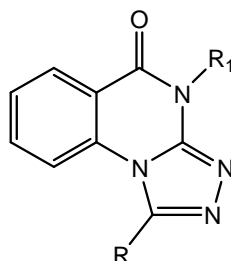
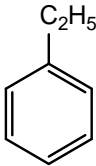
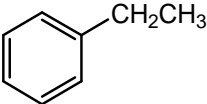



Fig.25

| S. No. | Substitutions | | Activity Reported |
|--------|-----------------|-------------------------------------------------------------------------------------|-------------------------|
| | R | R ₁ | |
| 25a. | CH ₃ |  | Antihistaminic activity |
| 25b. | CH ₃ |  | Antihistaminic activity |
| 25c. | CH ₃ |  | Antihistaminic activity |

CONCLUSION

Quinazolin-4-one is a unique template that is associated with several biological activities. This article high lightened research work of many researchers reported in literature for different pharmacological activities on quinazolin-4-one compounds synthesized. The review has presented comprehensive details of quinazolin-4-one analogues, potent compounds reported for particular pharmacological activity and the method or technique involved in evaluation process. More investigations must be carried out to evaluate more activities of quinazolin-4-one for many diseases whose treatment are difficult in the medical sciences.

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