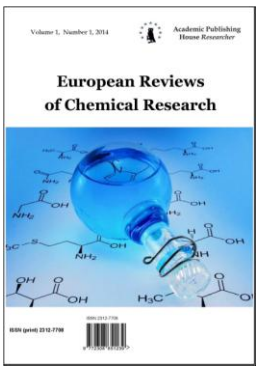
Published in the Russian Federation
European Reviews of Chemical Research
Has been issued since 2014.
ISSN: 2312-7708
E-ISSN: 2413-7243
Vol. 9, Is. 3, pp. 70-87, 2016

DOI: 10.13187/ercr.2016.9.70
www.ejournal14.com



Articles and Statements

UDC 544

A Review on a Highly Important Hetrocycle Quinazolinone Compounds and their Diverse Biological Activities

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Abstract

Quinazolinone 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 for their various pharmacological activities. Quinazolinone derivatives are one of the most active classes of compounds possessing a wide spectrum of biological activity. Recently several scientists have been reported that introduction of various heterocyclic moieties at quinazolinone nucleus modulate the activity. Various derivatives of quinazolinone have been synthesized and evaluated for their biological activities. This review might be helpful in the development of these novel lead molecules to potential drug candidates for future prospect.

Keywords: Quinazoline, antimicrobial, Anti HIV, Anti cancer, biologically active.

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. Quinazoline (**1**) are classes of fused heterocycles that are of considerable interest because of the diverse range of their biological activities such as, antimicrobial, anti-cancer, anticonvulsant, anti-tubercular, etc [1-5]. Quinazolin is a heterocyclic compound consists of two fused six membered simple aromatic rings, a benzene ring and a pyrimidine ring. The 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 (**2**) or quinazolinone are the most important classes of heterocyclic compounds. Quinazolin-4-one is synthesized when the keto group is introduced in the pyrimidine ring of quinazolin. Quinazolinone compounds possess versatile biological activities; such as anticancer [7-8], antitubercular [9], antibacterial [10], antifungal [11], anti-HIV [12], anthelmintic [13], anti-inflammatory [14] antihypertensive activities [15] and also other activities.

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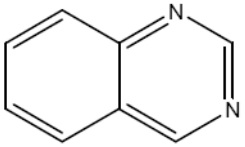
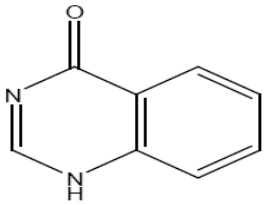


Quinazolin (**1**)

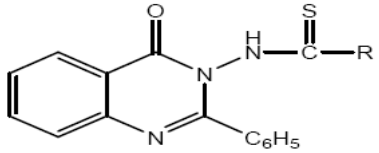


quinazolin-4-one (**2**)

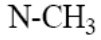
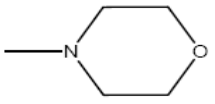
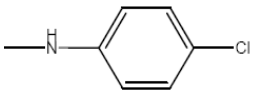
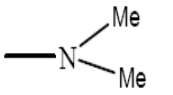
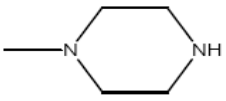
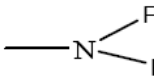
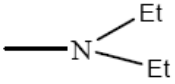
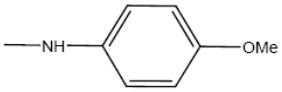
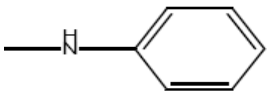
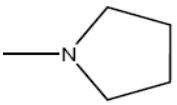
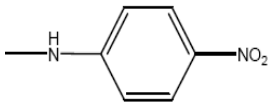
Pharmacological activities

The chemistry and pharmacology of quinazolinone have been of great importance to medicinal chemistry. Quinazolinones are versatile nitrogen containing heterocyclic compounds which are generally of little toxicity without side effects to human beings, and display a broad spectrum of biological activities like anticonvulsant and hypnotic [16], antimicrobial and antihistaminic [17], as well as antifungal activities [18].

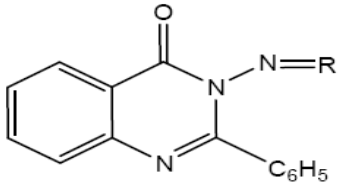
Analgesic and anti-inflammatory agents: Some quinazolin-4-one derivatives show promising analgesic and anti-inflammatory activities. The quinazoline derivatives might be beneficial in terms of biological activity for which further studies can be done to confirm it as a potential drug candidate. Some novel 2-phenyl-3-substituted quinazolin-4(3*H*) ones **(3a-k)** derivatives showed significant analgesic and anti-inflammatory activity compared with Diclofenac sodium as standard drug [19] compounds (3a-c) showed analgesic and anti-inflammatory acitivity and other compounds (3d-k) showed analgesic activity.



Compounds (3a-k)

Compd	R	Compd	R	Compd	R
3a		**3e**		**3i**	
3b		**3f**		**3j**	
3c		**3g**		**3k**	
3d		**3h**			

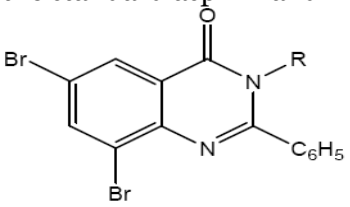
Quinazolinone fused Schiff bases **(4)** exhibited for anti-inflammatory activity [20].



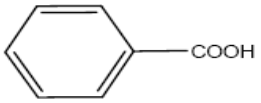
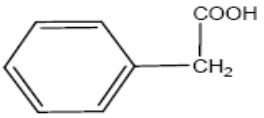
Compound 4a-f

Compd	Substitution (R)	Compd	R	Compd	R
4a	2-nitrobenzaldehyde	**4c**	Acetaldehyde	**4e**	2-chlorobenzaldehyde
4b	Cinnamaldehyde	**4d**	Furfuraldehyde	**4f**	3-OCH_3-4-OH-benzaldehyde

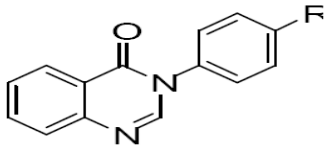
Quinazolin4-3(*H*)one compounds **(5)** showed analgesic and anti-inflammatory activity with varied potency when compared with the standard aspirin and indomethacin [22].



Compound 5a-b

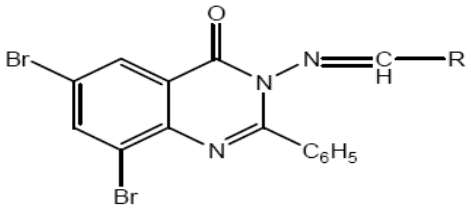
Compd	R	Compd	R
5a		**5b**	

Anti-microbial agents: Anti-microbials cover large spectrum biological activities like anti bacterial, anti fungal, anti viral, anti leshmanial, antiprotozoal, antiplasmodial etc. Several derivatives of quinazolins possess potential anti-microbial activities. However, the substitution pattern in quinazolinone nucleus at 2/3 position by different aryl or heteroaryl moieties markedly modulates its antifungal and other biological activities. The 4-(3H)-quinazolinone derivative (**6**) from the reaction of anthranilic acid and primary aromatic amines with Vilsmeier reagent in a few minutes under microwave irradiation providing good yields. All the quinazolinone compounds were screened for their *In vitro* anti fungal activity against *Candida Albicans, Aspergilles Niger*. Some of these compounds showed good antifungal activity than reference drug [21].

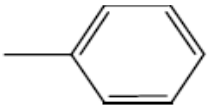
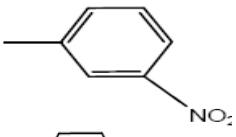
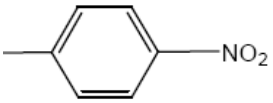
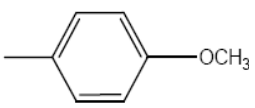
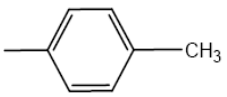
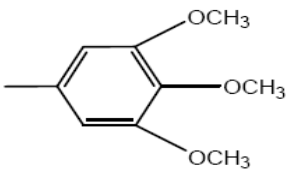


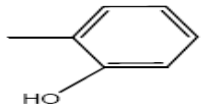
Compounds 6 (R= CH_3, Cl, NO_2, Br, OCH_3)**.**

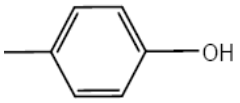
Some Schiff bases of 3-amino-6, 8-dibromo-2phenylquinazolin-4(3H)-ones (**7a-l**) and these compounds are screened as antimicrobial agents [22]. These compound were showed antifungal and antibacterial activity.

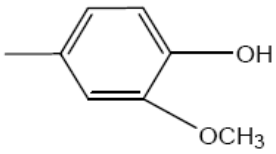


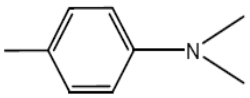
Compounds 7a-l

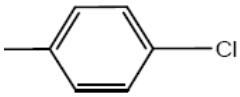
Compd	R	Compd	R	Compd	R
7a		**7e**		**7i**	
7b		**7f**		**7j**	

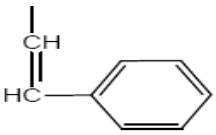
7c 

7g 

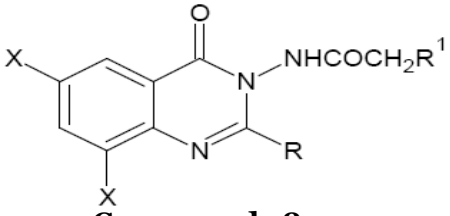
7k 

7d 

7h 

7l 

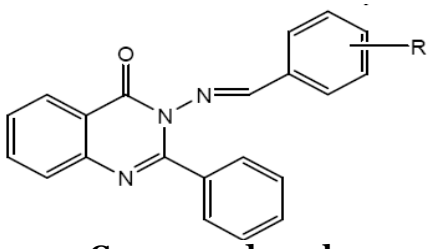
Some novel substituted 2-Imidazolyl-*N*-(4-oxoquinazolin-3(4*H*)-yl)-acetamides derivatives **(8a-p)** and evaluated the Antimicrobial activities [23].



Compounds 8a-p

Compd	X	R	R_1	Compd	X	R	R_1
8a	H	C_6H_5	Imidazolyl	**8i**	Br	CH_3	Imidazolyl
8b	H	C_6H_5	2-Methyl Imidazolyl	**8j**	Br	CH_3	2-Methyl Imidazolyl
8c	H	C_6H_5	2-Methyl benzi-imidazolyl	**8k**	Br	CH_3	2-Methyl benzi-imidazolyl
8d	H	C_6H_5	Benziimidazolyl	**8l**	Br	CH_3	Benziimidazolyl
8e	Br	C_6H_5	Imidazolyl	**8m**	Br	C_3H_7	Imidazolyl
8f	Br	C_6H_5	2-Methyl Imidazolyl	**8n**	Br	C_3H_7	2-Methyl Imidazolyl
8g	Br	C_6H_5	2-Methyl benzi-imidazolyl	**8o**	Br	C_3H_7	2-Methyl benziimidazolyl
8h	Br	C_6H_5	Benziimidazolyl	**8p**	Br	C_3H_7	Benziimidazolyl

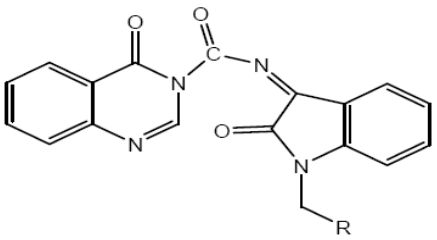
Some 3-(arylideneamino)-2-phenylquinazoline-4(3H)-ones derivatives **(9a-k)** exhibited antibacterial activity [24].



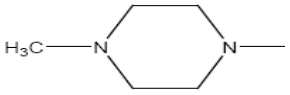
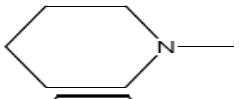
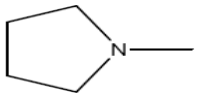
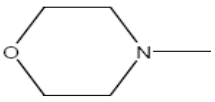
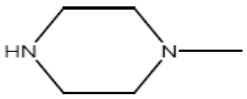
Compound 9-a-k

Compd	R	Compd	R	Compd	R	Compd	R
9a	2 –OH	**9d**	4 –N(CH_3)	**9g**	4–OH	**9j**	4 –NO_2
9b	4 –OCH_3	**9e**	4 –Cl	**9h**	4 –OCH_3	**9k**	H
9c	4 –F	**9f**	3 –OCH_3	**9i**	4–OH		

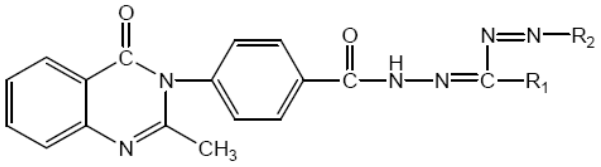
Some quinazolin-4-(3H)-one clubbed isatin derivatives (**10a-f**) exhibited antibacterial and antifungal activity [25].



Compounds 10a-f

Compd	R	Compd	R	Compd	R
10a		**10c**		**10e**	
10b		**10d**		**10f**	

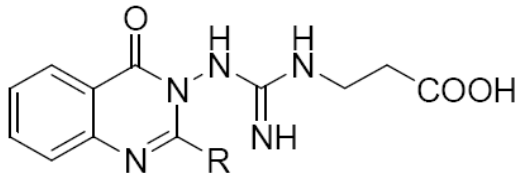
Several new quinazolinone formazans (**11**) which were evaluated for their antimicrobial, antifungal and antihelminthic property which were comparable to ciprofloxacin, fluconazole, albendazole and piperazine citrate respectively, some compounds were found to be potent [26].



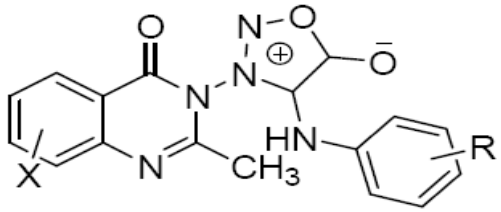
Compound 11a-c

Compd	R_1	R_2	Compd	R_1	R_2
11a	$C_6H_4NO_2$	C_6H_3FCl	**11c**	$C_6H_3(OH)(OCH_3)$	C_6H_3FCl
11b	$C_6H_4N(CH_3)_2$	C_6H_4Cl			

A series of 3-[3-(2-Substituted-4-oxo-4Hquinazolin-3-yl)-guanidino]-propionic acid derivatives (**12**) have been synthesied. Some compounds were more potent against *Monascus puppures, Aspergillus fumigates, A. parasiticus* and *Microsporum gypseum* than the reference drug Clotrimazole [27]. 2-methyl-3[sydnon-4-substitutedaniline-3'-yl] mono substituted quinazolin-4-(3H)-one (**13**) were synthesized. All the compounds and the reference drugs fluconazole and griseofulvin were evaluated for antifungal against different strains of fungi. *C. albicans*, *C. parapsilosis*, *A. fumigatus* and *A. niger* and showed equipotency towards *C. krusei* [28].

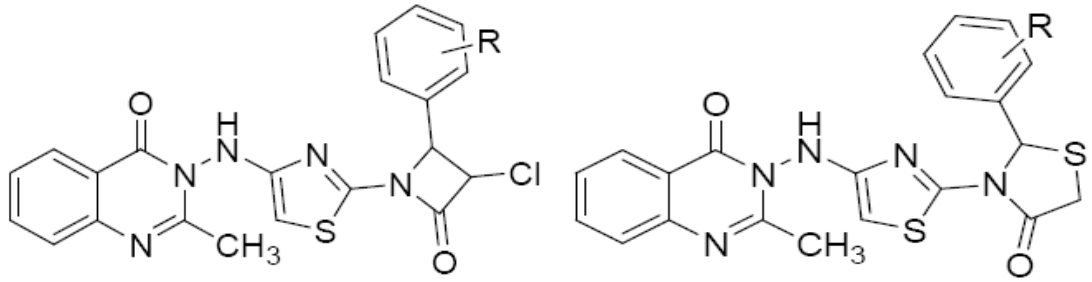


Compound 12
R= CH_3, C_6H_5, 4-$OCH_3C_6H_4$.



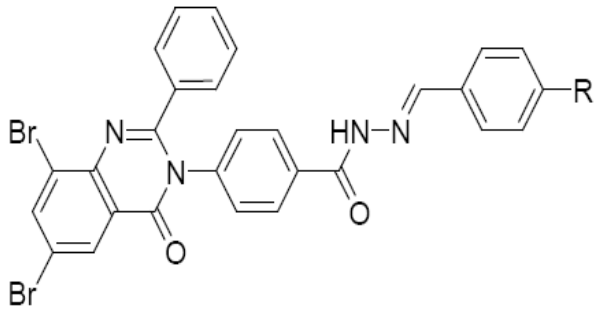
Compound 13
X= H, 6 Br; **R**= H, o-OCH3, p-OCH3, o-Cl, p-Cl

Compound 3-[2-(3-Chloro-2-oxo-4-Ar-azetidin-1-yl)-thiazol-4-ylamino]-2-methyl-3H-quinazolin-4-ones and 2-Methyl-3-(4'-oxo-2'-substutedphenyl-thiazolidin-3-ylamino)-3H-quinazolin-4-ones (**14**) were screened for their antifungal activity aganist *A. fumigates, A. niger, C. albicans* and *A. Flavus* [29].



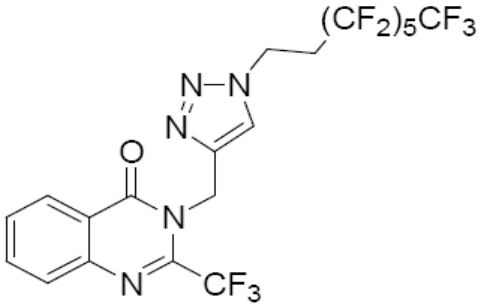
Compound 14a-b **R**=H, o-OH, p-OH, o-CH_3, p-OCH_3.

Novel 6,8-dibromo-4(3H)quinazolinone derivatives (**15**) were found to exhibit the most potent *in vitro* anti-fungal activity [30]. A series of perfluoroalkyl-1H, 1,2,3- triazol-4-yl substituted quinazolines (**16a-b**) were exhibited antimicrobial and antifungal activity [31]. 4-(Substitutedphenyl)-1-(aryl)-3a,4-dihydro-1H-[1,2,4]triazolo[4,3-a]quinazolin-5-ones (**17**) have been tested for their antifungal activity aganist *A. niger* and phytophora. Interoduction of OCH_3, OH and Cl groups to the hectrocyclic frame work enhence the antifungal activity [32].

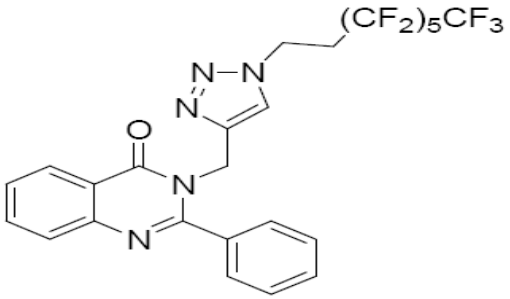


Compound 15

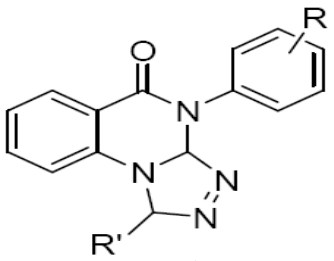
R= 4-OCH_3, 4-CH_3, 2-OH.



Compound 16a

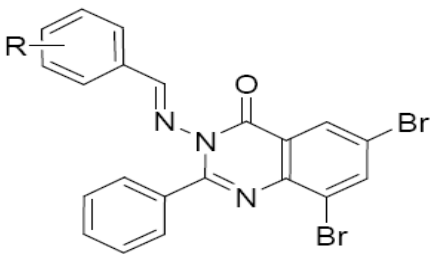


Compound 16b



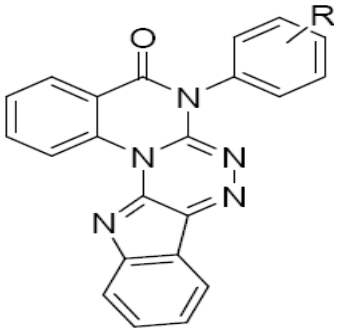
Compound 17 **R**=4-CH_3, 4-OCH_3, 4-Cl, 4-Br; **R'**= 4-$OCH_3C_6H_4$, 2- $NO_2C_6H_4$, 2-ClC_6H_4, 4-ClC_6H_4, 2-OHC_6H_4, 4-OHC_6H_4.

Anti-microbial studies of novel Schiff bases of 3-amino-6,8-dibromo-2-phenylquinazolin-4(3*H*)-ones (**18**) were described against the Gram positive, Gram-negative and fungi strains [33]. Quinazolinones (**19**) derivatives were screened for their antimicrobial activity against bacterial and fungal strain



Compound 18

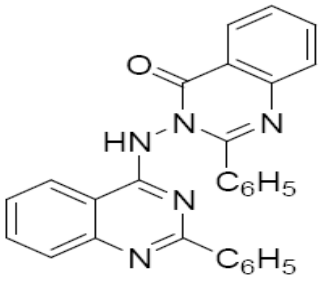
R= 4-OCH_3, 2-OH, 4-OH, 4-Me, 4-Cl,4-NO_2



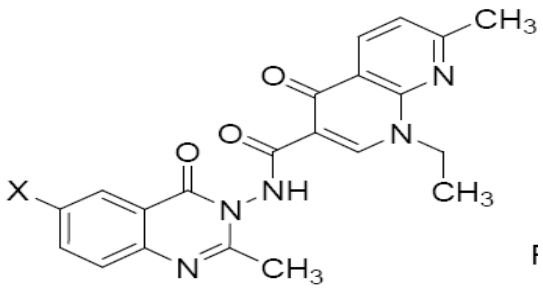
Compound 19

R= H, 4-Me, 4-OMe, 4-Cl

A novel 2,3- substituted quinazolinon derivatives (**20**) were screened for their antifungal activity [34]. Quinazolone derivatives (**21**) of nalidixic acid showed potential antibacterial and antifungal activity [35].

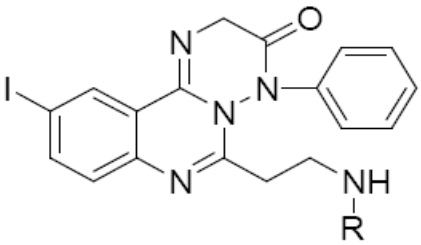


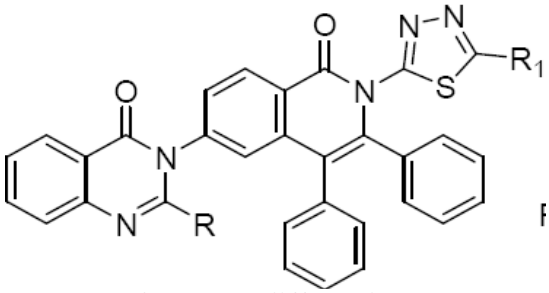
Compound 20



Compound 21 X= H, I, NO_2.

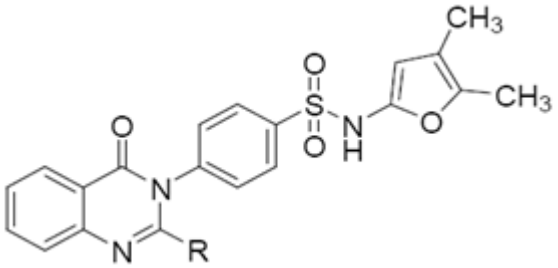
Some heterocyclic derivatives of quinazolinones (**22**) and (**23**) were assayed for their antifungal activitie. Some of these derivatives have shown good antifungal activity aganist fungal strain [37, 37].



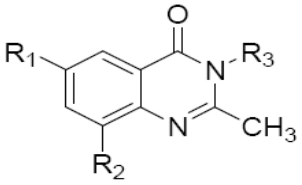


Compound 22 R= diff. Heterocycles. **Compound 23** R_1 = diff. Aryl groups, R = H.

Antifungal activity exhibited by of some novel 6-bromo-2-methyl/phenyl-3-(sulphonamido) quinazolin-4(3H)-ones (**24**) were evaluated [38]. A series of 2-methylquinazolin- 4(3H)-ones (**25**) were exhibited antifungal activity [39].

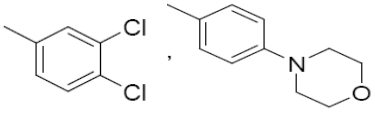


Compound 24

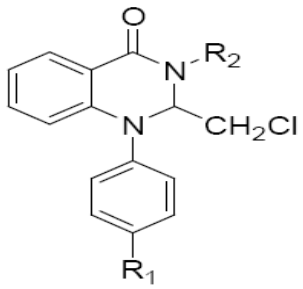


Compound 25

R=CH_3, C_6H_5 R_1 =H, Br R_2 =H, Br R_3 =

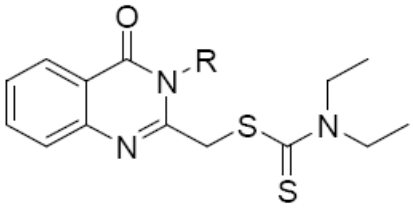


Some new 1-substituted-2-(chloromethyl)-4-(1H)-quinazolinones (**26**) were synthesized and screened for their antifungal activity [40]. In-vitro antifungal activity aganist fungal strain and synthesis of some analogues of 2-methyl quinazolinones (**27**) were reported [41].



Compound 26

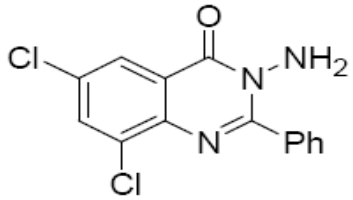
R_1 =H, NO_2, OCH_3. R_2 = Substuted Ar



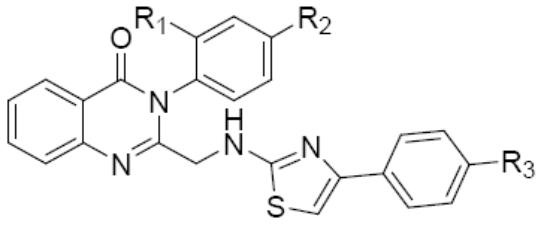
Compound 27

R= H, 4-$CH_3C_6H_4$, 4-ClC_6H_4.

Significant antifungal activity was observed for new 6,8-dichloro-2-phenyl-4-(3H)-quinazolinone (**28**) compound [42]. A series of 3-aryl-2-(4´-arylthiazol-2´-yl aminomethyl)-quinazol in-4(3H)-ones (**29**) have been elicited for their impressive fungicidal activities [43].

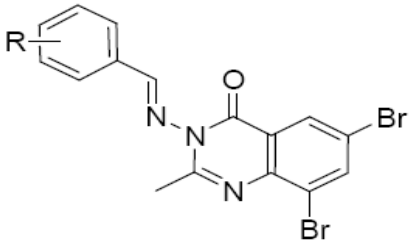


Compound 28



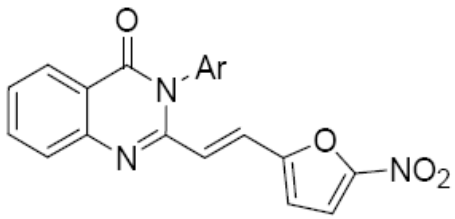
Compound 29 R_1, R_2, R_3= H, Cl, OCH_3 etc

New 2,3- and 2,4-disubstituted quinazoline (**30**) derivatives showed potential antibacterial and antifungal activity [44]. 3-Aryl-2-[(5-nitro-2-furfuryl)vinyl]quinazolin-4-ones (**31**) were exhibited fungicidal activity [45].



Compound 30

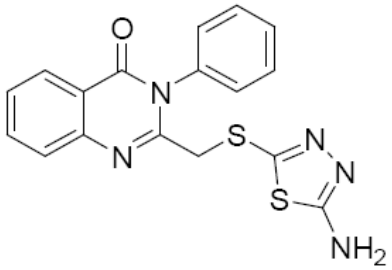
R= 2,4-Cl, 4-OH.



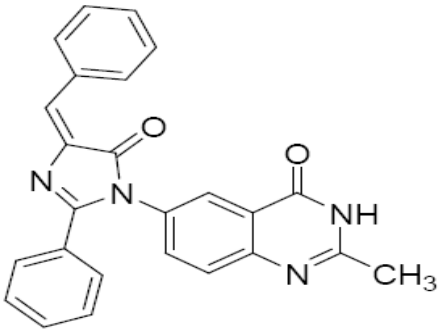
Compound 31

Ar= Ph, 4-ClC_6H_4, 4-$CH_3C_6H_4$, 3-$CH_3C_6H_4$, 4-$OCH_3C_6H_4$.

Pharmacological screening of some quinazolinones (**32**) displayed activity against various fungal species [46]. Compound 6-(4´-substituted-benzylidene-2´-methyl /phenyl-5´-imidazolinon-1´-yl)-2-methyl-4(3H)-quinazolinone (**33**) and assessed the compounds for their antifungal activity against *A. niger* [47].



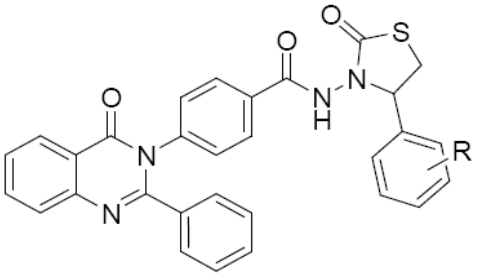
Compound 32



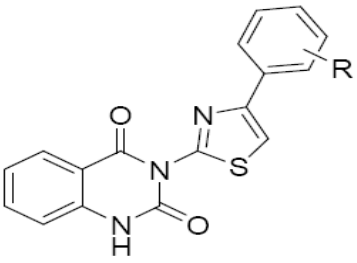
Compound 33

Potent antifungal activity in some newer quinazolinones (**34**) containing thiazolidinone moiety was reported [48]. 3-(4'-aryl-2'-thiazolyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazolinones (**35**)

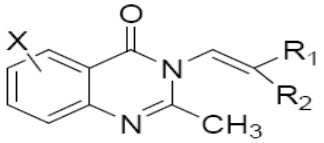
as promising antifungal agents [49]. Some Schiff bases of 3-amino-2-methylquinazolin-4(3H)-ones (**36**) were evaluated for their antifungal activity [50].



Compound 34
R= Cl, OCH_3, H etc.

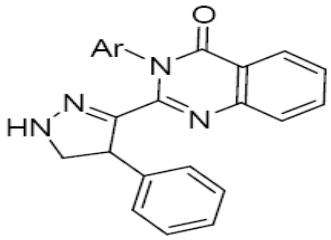


Compound 35
R= 4-Br, 2-Cl, H, 4-Me.

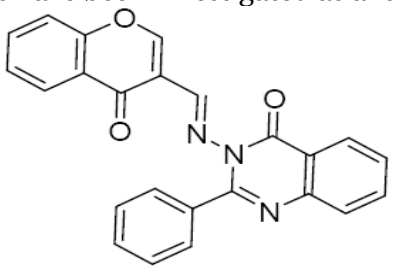


Compound 36
X= H, Br; R_1= H, Me, Ph; R_2= Ph, 2-$OCH_3C_6H_4$.

2-(4-aryl-2-pyrazolin-3-yl)-3-aryl-4(3H)-quinazolinones (**37**) have been prepared by cycloaddition of diazomethane. Some of these compounds have been found to exhibit good antifungal activity [51]. A condensation of four defferent 3-formylchromones with 2-methyl/phenyl-3-amino-4(3H)-quinazolinone and their dibromo analogs have been characterized as their respective 3-[N-(4-oxo-2-methyl/phenyl-3-quinazolinyl)-formimidoyl]-chromones (**38**). These compounds have been investigated as antifungal agent [52].

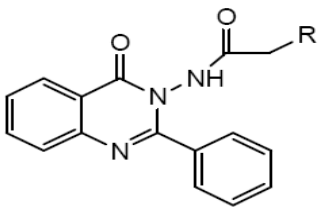


Compound 37

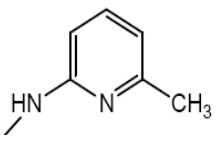
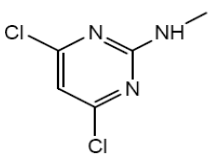
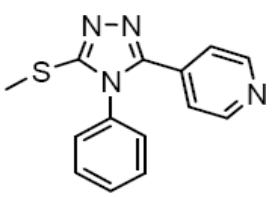
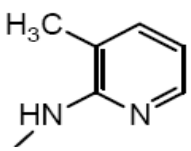
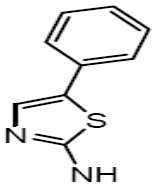
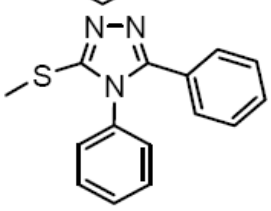


Compound 38

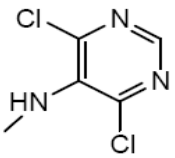
Antitubercular agents: There are no promising quinazolines marketed presently in the category of tuberculosis (TB). But several novel molecules have been synthesized in the past which showed promising results but unfortunately could not make it up to the marketing stage. Some 2-phenyl-3-substituted quinazolin-4(3*H*)-ones **(39a-g)** were exhibited anti-TB and antioxidant activities [53].



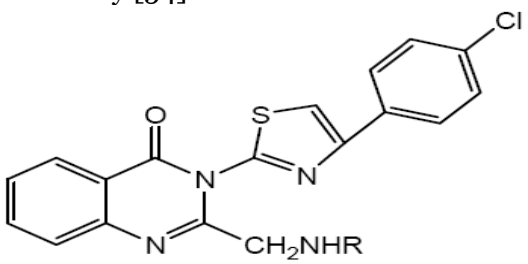
Compound 38a-g

Compd	R	Compd	R	Compd	R
38a		**38d**		**38f**	
38b		**38e**		**38g**	

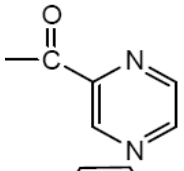
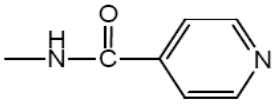
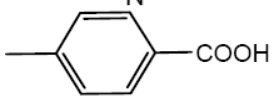
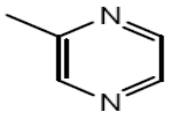
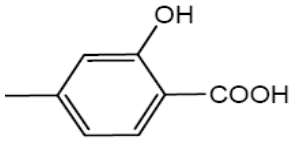
38c



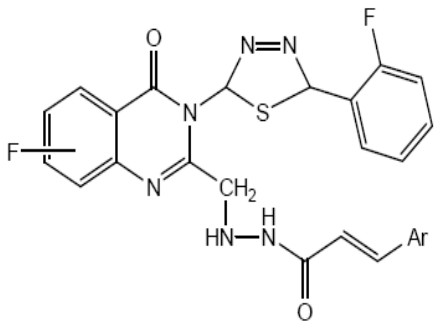
The N-3(4-(4-chlorophenyl thiazol-2-yl)-(2-(amino) methyl) quinazolin4(3H)-one **(39a-j)** and their derivative for anti-TB activity [54].



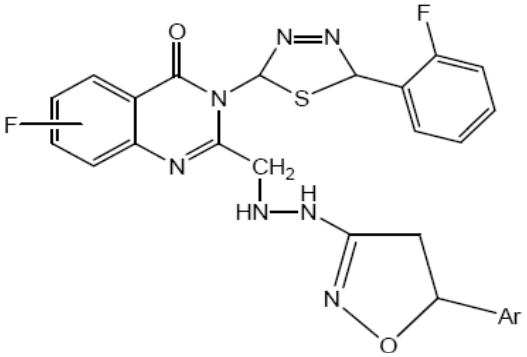
Compound 39a-j

Compd	R	Compd	R	Compd	R
39a	C_6H_4Cl	**39e**	$C_6H_4OCH_3$	**39h**	
39b	C_6H_4F	**39f**		**39i**	
39c	$C_6H_4NO_2$	**39g**		**39j**	
39d	$C_6H_4CH_3$				

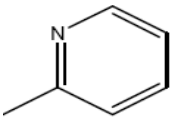
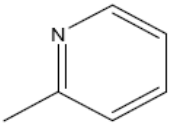
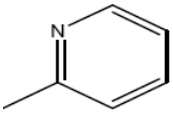
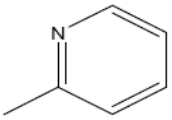
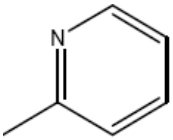
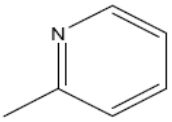
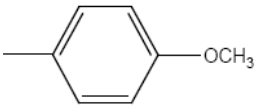
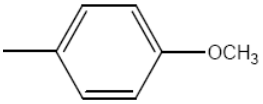
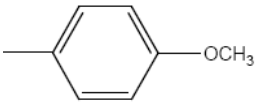
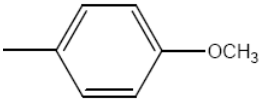
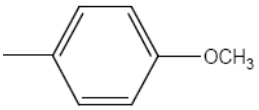
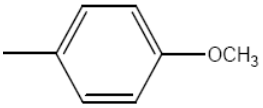
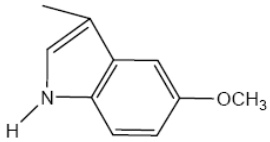
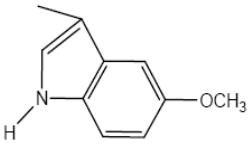
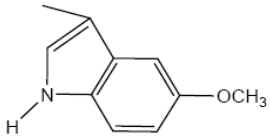
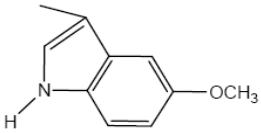
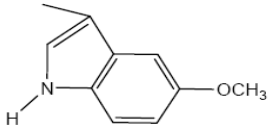
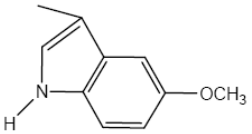
Anticonvulsant agents: Some quinazolinone derivatives showed promising anticonvulsant activities. For the future prospect quinazolinone can be the suitable candidate for the treatment of convulsions. Various thiadiazolylpyridinyl (**40a-i**) /indolylisoxazolyl (**41a-i**) quinazolinone-4-ones showed antconvulsant anti-psychotic activity [55].



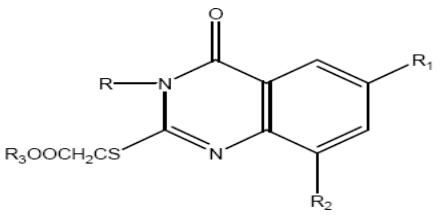
Compound 40a-i



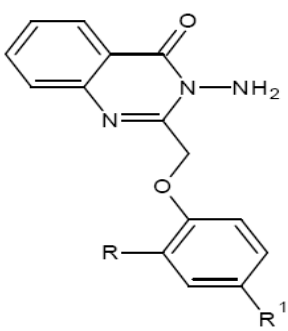
Compound 41a-i

Compd	R_1	R_2	Compd	R_1	R_2
40a	**H**		**41a**	**H**	
40b	**6-Br**		**41b**	**6-Br**	
40c	**6,8-Br**		**41c**	**6,8-Br**	
40d	**H**		**41d**	**H**	
40e	**6-Br**		**41e**	**6-Br**	
40f	**6,8-Br**		**41f**	**6,8-Br**	
40g	**H**		**41g**	**H**	
40h	**6-Br**		**41h**	**6-Br**	
40i	**6,8-Br**		**41i**	**6,8-Br**	

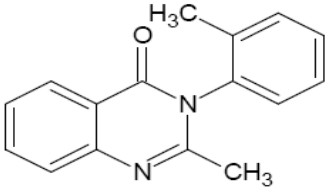
Some derivatives of 3*H*-quinazolin-4-one **(42)** through condensation reaction of their potassium salts with methyl, ethyl and phenyl isocyanate and synthesized compounds showed promising anticonvulsant activity [56]. Quinazolin-4-(3*H*)-one derivatives (**43**) were showed Anticonvulsant activity [57]. The 3,4-Dihydro-4-oxoquinazolin derivative (**44,45**) were exhibited anticonvulsant activity [58].



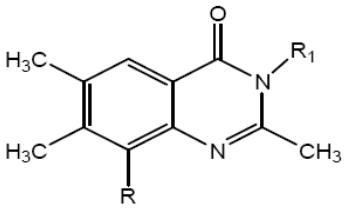
Compound 42
R=CH_3 R_1=H R_2=H R_3=C_6H_5



Compound 43 **R_1=H R_2=Cl**



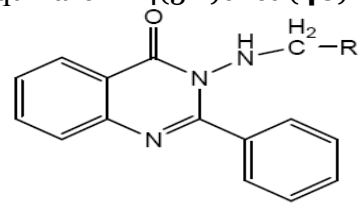
Compound 44



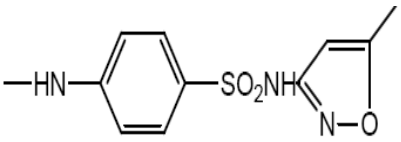
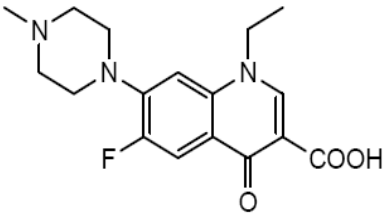
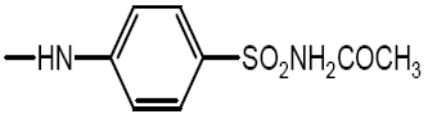
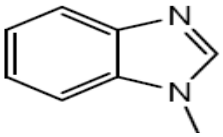
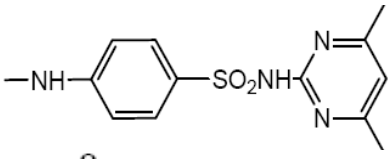
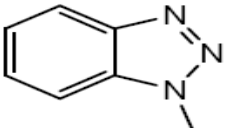
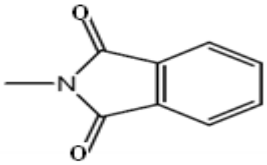
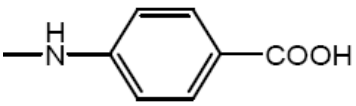
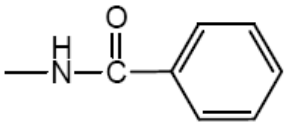
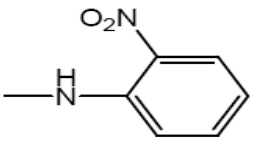
Compound 45

R=COOH, **R₁**= p-C_6H_5

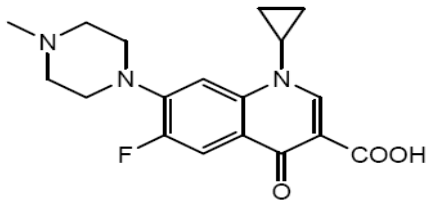
Anti HIV agents: Quinazolin-4-(3H)-one is a versatile lead molecule for the design of potential bioactive agents. The anti-HIV activity of 2-phenyl-3-substituted quinazolin-4-(3H)-ones. the 2-phenyl-3-substituted quinazolin-4-(3H)-ones [59-61]. A large number of quinazolines have been synthesized and studied for wide range of anti-viral activity. Some 2-phenyl 3-substituted quinazolin-4(3H)ones (**46**) were showed antiviral/ anti-HIV activity [62].



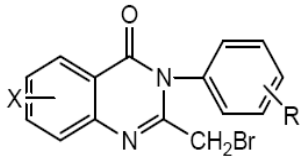
Compounds 46a-k

Compd	R	Compd	
46a		**46g**	
46b		**46h**	
46c		**46i**	
46d		**46j**	
46e		**46k**	

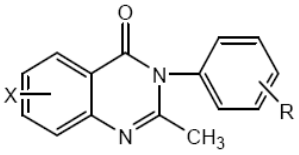
46f



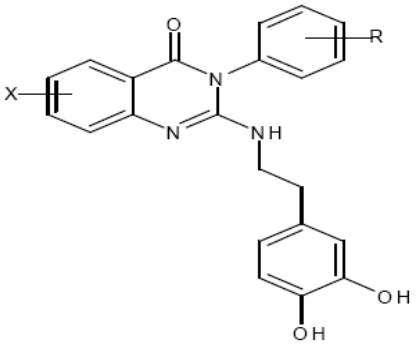
Antiparkinson agents: Parkinsonism is caused due to deficiency of dopamine. After the attachment of dopamine with some quinazolin derivative shows promising antiparkinson activity. Series of 3-substituted phenyl 2-(3,4-dihydroxy phenyl ethyl amino)-6-substituted quinazolin-4-(3H) ones **(47a-h, 48a-h and 49a-h**) 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 [63]. 34



Compound 47a-h



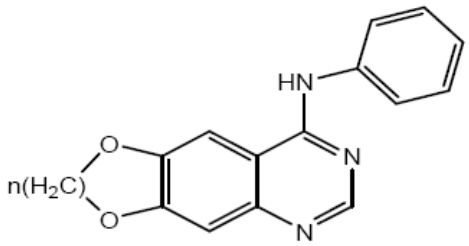
Compound 48a-h



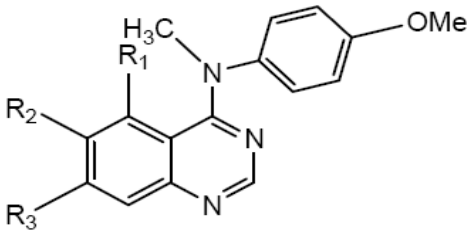
Compound 49a-h

Compd	X	R	Compd	X	R	Compd	X	R
47a	H	H	**48a**	H	H	**49a**	**H**	H
47b	H	2-Cl	**48b**	H	2-Cl	**49b**	**H**	2-Cl
47c	H	4-OCH_3, 2-CH_3	**48c**	H	4-OCH_3, 2-CH_3	**49c**	**H**	4-OCH_3, 2-CH_3
47d	H	2-OCH_3	**48d**	H	2-OCH_3	**49d**	**H**	2-OCH_3
47e	Br	H	**48e**	Br	H	**49e**	**Br**	H
47f	Br	2-Cl	**48f**	Br	2-Cl	**49f**	**Br**	2-Cl
47g	Br	4-OCH_3, 2-CH_3	**48g**	Br	4-OCH_3, 2-CH_3	**49g**	**Br**	4-OCH_3, 2-CH_3
47h	Br	2-OCH_3	**48h**	Br	2-OCH_3	**49h**	**Br**	2-OCH_3

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. Several dioxolane, dioxane (**50**), 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 [64]. Several N-methyl-4-(4-methoxyanilino) quinazolines (**51**) 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-positioncan be replaced by a nitrogen and thenitrogen at the 3-position can be replaced by a carbon. The following compounds were found to be potent when compared with standard Azixa [65].

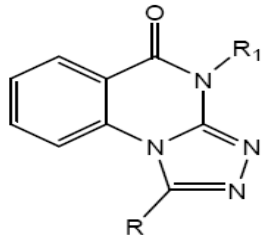


Compound 50

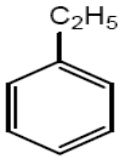
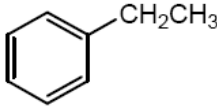
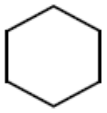


Compound (51a-b) R_1 **a,b** =H; R_2, **a**=NH_2, **b**=NO_2; R_3 **a, b =H**

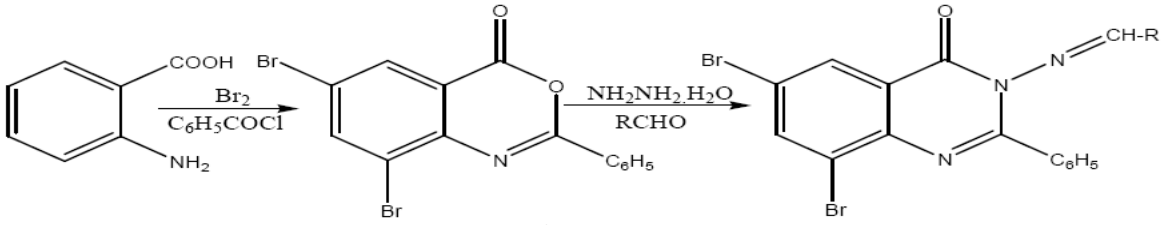
Anti-Histaminic agents: Some quinazoline possess good antihistaminic properties. Several 4-(3-ethylphenyl)-1-substituted-4*H* [1,2,4] triazolo [4,3-*a*] quinazolin-5-ones,4-(4-ethylphenyl)-1-substituted-substituted-4*H* [1,2,4] triazolo [4,3-*a*] quinazolin-5-ones and 1-substituted-4-cyclohexyl-4H-[1,2,4] triazolo [4,3-a] quinazolin-5-ones [66-68]. It was found that by varying substitution over the first position of the triazolo quinazoline (**52**) 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.



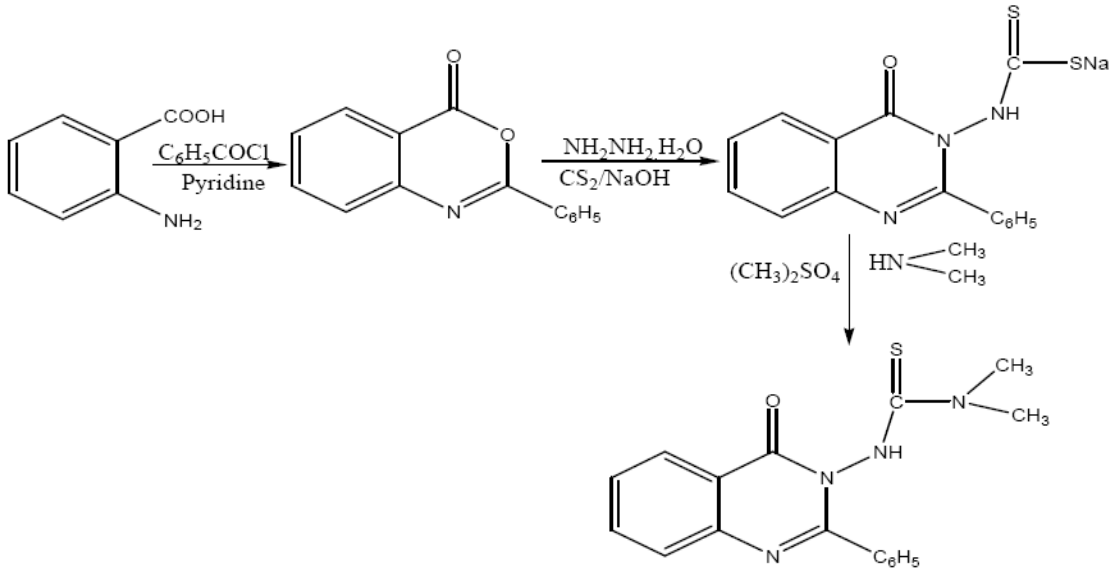
Compound 52

Compd	R_1	R_2	Compd	R_1	R_2	Compd	R_1	R_2
52a	CH_3		**52b**	CH_3		**52c**	CH_3	

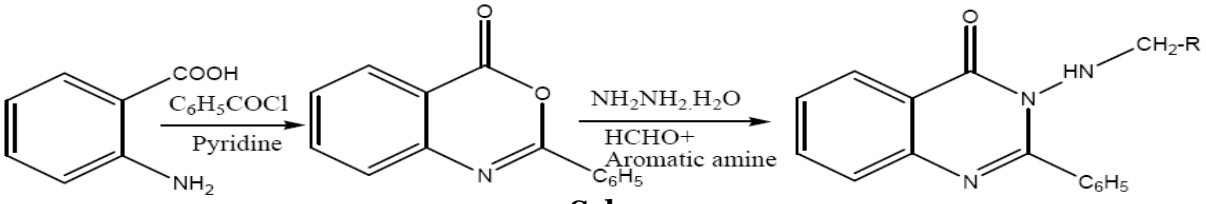
Chemistry: Various methods have been proposed by various researchers for the synthesis of quinazolin-4-ones as mentioned below. Anthranilic acid is the key reagent for the synthesis of quinazolin-4-ones. Some Schiff bases of 3-amino-6, 8-dibromo-2 phenylquinazolin-4(3H)-ones (Scheme 1) [69], some novel 2-phenyl-3-substituted quinazolin-4(3*H*)ones (Scheme 2) [70], some 2-phenyl 3-substituted quinazolin-4(3*H*)-ones derivatives (Scheme 3) [71], synthesized quinazolinone fused Schiff bases (Scheme 4) [72], synthesized novel quinazolinone derivatives (Scheme 5) [73] and synthesis of ethyl 2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl) acetate as important analog and intermediate of 2,3 disubstituted quinazolinones (Scheme 6) [74].



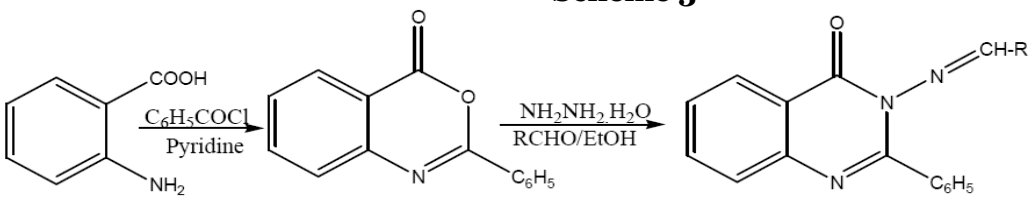
Scheme 1



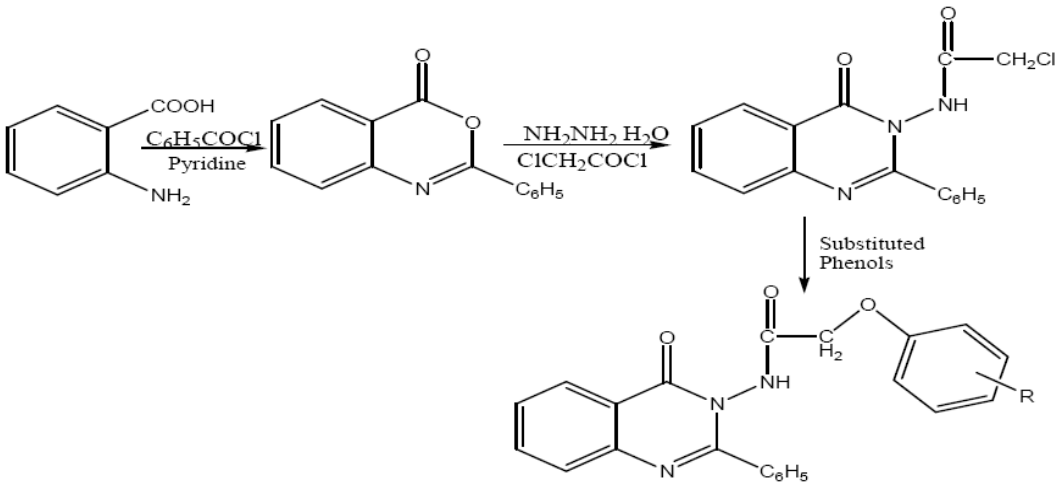
Scheme 2



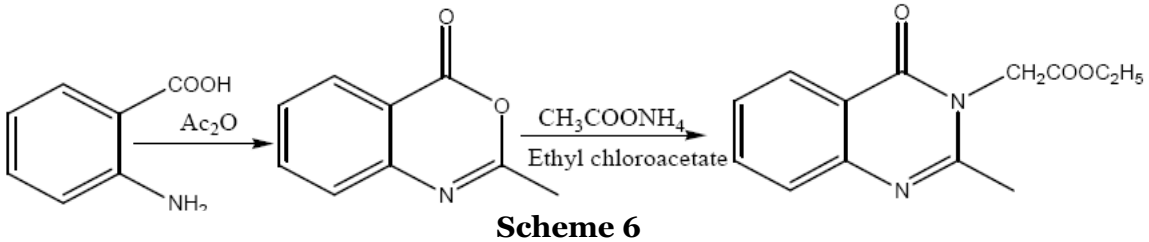
Scheme 3



Scheme 4



Scheme 5



Scheme 6

Conclusion

Quinazolinone 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 quinazolinone compounds synthesized. The review has presented comprehensive details of quinazolinone 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 quinazolinone for many diseases whose treatment are difficult in the medical sciences. The literature reveals that the synthesized quinazoline compounds exhibited good biological activities. Several works found that substituted quinazolenone containing different heterosystems which were found to posses potent biological activities [75, 76]. By the present scenario it can be concluded that substituted quinazolenones have a great potential which remain to be disclosed till date.

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