Int J Pharm Bio Sci 2012 Oct; 3(4): (P) 119 - 132

Review Article **Medicinal chemistry**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

A REVIEW : QUINAZOLIN-4-ONES AS ANTIFUNGAL AGENTS

CHATRASAL SINGH RAJPUT* AND PUSHKAR SINGH BORA

Synthesis Department, Jubilant Chemsys Ltd. R & D B-34, Sector 58, Noida 201301, U P, India

ABSTRACT

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 2 and 3 position of quinazolinone nucleus modulate the antifungal activity. Various derivatives of quinazolinone have been synthesized and evaluated for their antifungal activity against *Candida Albicans, Aspergilles Niger, Aspergillus Clavatus, Aspergillus Fumigatus, Aspergillus Parasiticus* at various concentrations. This article is sincere attempt to review chemistry and antifungal activity of quinazolinones for last 20 year (1991-2011).

KEYWORDS: Quinazolinones and antifungal activity.

CHATRASAL SINGH RAJPUT
Synthesis Department, Jubilant Chemsys Ltd. R & D B-34, Sector 58, Noida 201301, U P, India
Tel.: +919811816159
E-mail address: chatrasalrajput@gmail.com

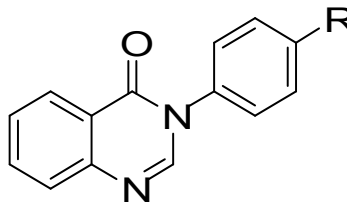
Corresponding author

INTRODUCTION

Fungi are heterotrophic microorganisms that are dependent upon organic compounds for their nutrition. These are characterized by absorptive type of nutrition i.e. these feed by excretion of enzymes into the substrate and by subsequent take up of digested compounds through the cell wall. These differ from the bacteria in being 'eukaryotes' because their genome is organized in a nucleus surrounded by a cell wall. The word 'fungi' is a general term which includes both yeasts and molds and occupy an amazing variety and number of ecological niches. They fulfill a critical function in nature by converting such polymers lignin, chitin, and cellulose into humus. Fungal infections pose major problem in immunocompromised patients. Problems have continued to aggreviate during past 20 years and are now significant causes of morbidity and mortality. This is particularly true in patients with hematological malignancies undergoing induction or consolidation chemotherapy, in patients with acquired immunodeficiency secondary to infection by human immunodeficiency viruses, and in immunosuppresed organ transplant recipients. Patients with diabetic ketoacidosis are also at great risk. These infections also occur in some iatrogenic or nosocomial settings. Autopsy data indicate that more than half of the patients who die with malignancies are infected with *Candida* species, approximately one-third with *Aspergillus* spp. and substantial number with *Cryptococcus* spp.or other fungi such as *Fusarium* spp. Major factor which peridispose patients to invasive fungal diseases include: prolonged neutropenia (chemotherapy-induced); defective T-lymphocyte function (associated with organ transplantation and HIV infection); impaired macrophage function, particularly of pulmonary macrophages (associated with high doses and prolonged administration of corticosteroids); and barrier defects (associated with invasive medical procedures, vascular catheters, parenteral nutrition as also haemodialysis and peritoneal dialysis) in compromised patients.

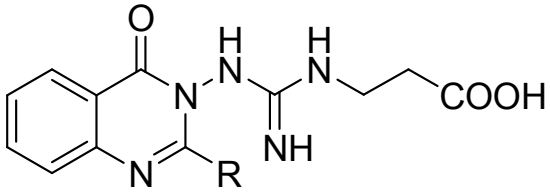
Although invasive fungal diseases are now more frequent than during the first half of the 20th century, they are still difficult to diagnose clinically. During the latter half of the century, particularly during the past two decades, a number of different classes of antifungal agents have been discovered. The recent spurt in antifungal drug research has occurred because there is a critical need for new antifungal agents to treat these life-threatening invasive infections. Since the discovery of amphotericin B, there has been rapid progress in the field, and we have newer agents that are available for clinical use like ketoconazole, fluconazole, griseofulvin, clotrimazole, flucytosine, nystatin etc., their clinical efficacy in some invasive fungal infections, such as *aspergillosis* and *furiosis,* is not optimal. Thus, intense efforts in antifungal drug discovery are still needed to develop more promising and effective antifungal agents for use in clinical arena. With a view to develop potent antifungal agents, newer derivatives of hectrocyclic moieties like quinazolinone (Selvam et al., 2004; Paneersalvam et al., 2003); pyridine (Popat et al., 2004; Raj and Rao, 2003), and coumarin (Rajanarendar et al., 2004; Soroush et al., 1999) etc were prepared. Further, the antifungal compounds were then synthesized by incorporating various congeners like thiazole (Rajanarendar et al., 2004,), thiadiazole (Matysiak and Malinski 2007), sydnone (Yelamaggad et al., 1995; Bekhit et al 2001, Moustafa and Eisa 1992), azetidinone (Pandey et al., 2005, and Vasoya et al., 2005), and thiazolidinone (Patel et al., 2006, Bhusare et al., 2004;) around these basic nuclei, which were also reported to possess antifungal activity by several scientists as given in review of the literature 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 (Nagwa et al., 2011), antimicrobial and antihistaminic (Omar et al., 1991), as well as antifungal activities (Selvam et al., 2004). 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. Further, the antifungal potency of quinazolinones is proved by synthesizing the following compounds by various scientists. Structures of all these compounds were established on the basis of elemental (C,H,N) and spectral (IR, ^{1}H-NMR and mass spectral data) analysis and screened for their antifungal activity. Priya et al (2011) synthesized 4-(3H)-quinazolinone derivative (Fig. 1) 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 synthesized quinazolinones 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.



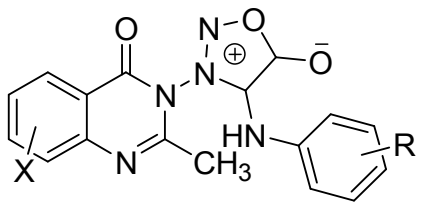
R= CH_3, Cl, NO_2, Br, OCH_3 etc.
Figure 1

A series of 3-[3-(2-Substituted-4-oxo-4H-quinazolin-3-yl)-guanidino]-propionic acid derivatives (Fig. 2) have been synthesied by Palani and Vijay 2011. All the synthesized compounds were characterized by IR, 1HNMR and mass spectra. Some of synthesized compounds were more potent against Monascus puppures, Aspergillus fumigates, Aspergillus parasiticus and Microsporum gypseum than the reference drug Clotrimazole.



R= CH_3, C_6H_5, 4-$OCH_3C_6H_4$ etc.
Figure 2

2-methyl-3[sydnon-4-substitutedaniline -3'-yl] mono substituted quinazolin-4-(3H)-one (Fig. 3) were synthesized by Rajput et al (2011). All the compounds and the reference drugs fluconazole and griseofulvin were evaluated for antifungal against different strains of fungi. *C.albicans*, *C.albicans ATCC, C.parapsilosis* 22019, *A. fumigatus* and *A. niger* and showed equipotency towards *C.krusei.*

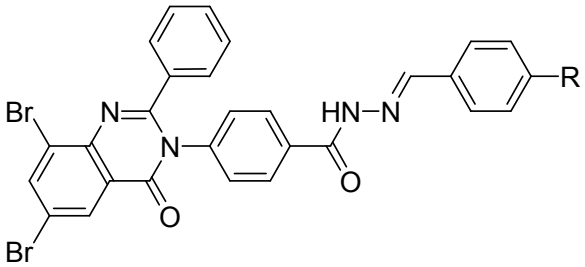


X= H, 6 Br; R= H, o-OCH_3, p-OCH_3, o-Cl, p-Cl ect.
Figure 3

Rajput et al (2010) synthesised 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 (Fig. 4). All the newly synthesized compounds were screened for their antifungal activity aganist Aspergillus fumigates, Aspergillus niger, Candida albicans and A. Flavus.

R=H, o-OH, p-OH, o-CH_3, p-OCH_3 etc.
Figure 4

Novel 6,8-dibromo-4(3H)quinazolinone derivatives (Fig 5) were synthesised by Mosaad (2010) and were found to exhibit the most potent *in vitro* anti-fungal activity.



R= 4-OCH_3, 4-CH_3, 2-OH etc.
Figure 5

A series of novel perfluoroalkyl-1H, 1, 2, 3-triazol-4-yl substituted quinazolines (Fig 6) were synthesized by Mani et al (2011) and screened for antimicrobial activity to identify potential compounds. The formation of products predicted by optimizations at B3LYP/6-31G* level, was analyzed kinetically and thermodynamically.

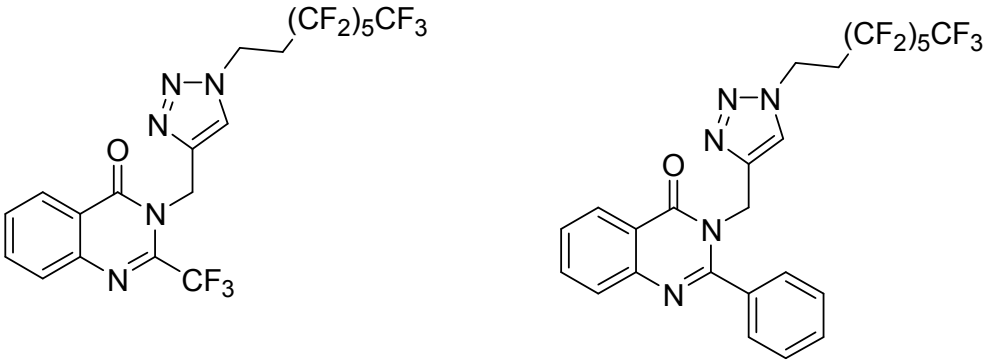
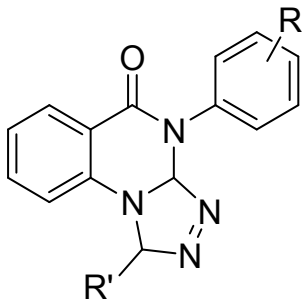


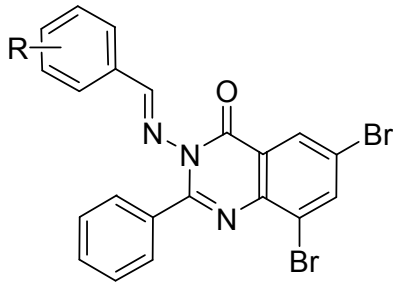
Figure 6

4-(Substitutedphenyl)-1-(aryl)-3a,4-dihydro-1H-[1,2,4]triazolo[4,3-a]quinazolin-5-ones (Fig 7) have been synthesised by Deshmukh et al (2010). All newly synthesised compounds have been tested for their antifungal activity aganist Aspergillus niger and phytophora. Interoduction of OCH_3, OH and Cl groups to the hectrocyclic frame work enhence the antifungal activity.



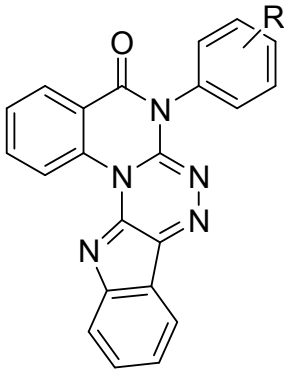
R=4-CH$_3$, 4-OCH$_3$, 4-Cl, 4-Br;
R'= 4-OCH$_3$C$_6$H$_4$, 2- NO$_2$C$_6$H$_4$, 2-Cl C$_6$H$_4$, 4-ClC$_6$H$_4$, 2-OH C$_6$H$_4$, 4- OH C$_6$H$_4$ etc.
Figure 7

Synthesis, characterization and anti-microbial studies of novel Schiff bases of 3-amino-6,8-dibromo-2-phenylquinazolin-4(3*H*)-ones (Fig 8) were described against the standard Gram-positive, Gram-negative and fungi strains by Perumal et al 2009.



R= 4-OCH$_3$, 2-OH, 4-OH, 4-Me, 4-Cl,4-NO$_2$ etc.
Figure 8

A novel quinazolinones (Fig 9) derivatives were synthesized and screened for their antimicrobial activity against bacterial and fungal strain. (Sarvesh et al 2009)



R= H, 4-Me, 4-OMe, 4-Cl etc.
Figure 9

A novel 2,3- substituted quinazolinon derivatives (Fig 10) were synthesized Anjani et al 2007 and screened for their antifungal activity. Gaurav and Kini (2006) synthesised and evaluated of new quinazolone derivatives (Fig 11) of nalidixic acid as potential antibacterial and antifungal agents .

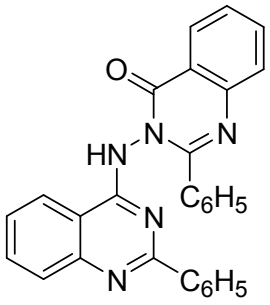


Fig 10

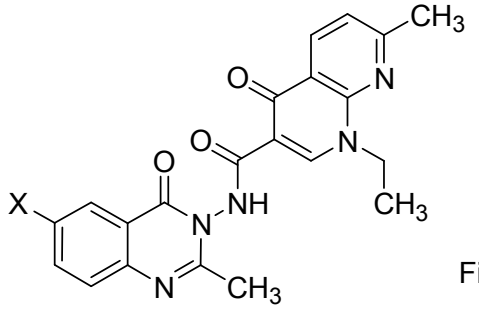


Fig 11

X= H, I, NO2.

Singh et al. (2006) (Fig 12) and Pandey et at (2005) (Fig 13) synthesized some heterocyclic derivatives of quinazolinones and also assayed them for their antifungal activitie. Some of these derivatives have shown good antifungal activity aganist fungal strain.

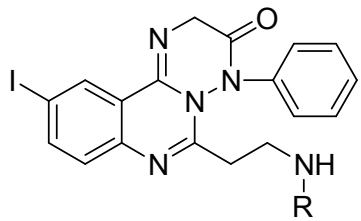


Fig 12

R= diff. Heterocycles.

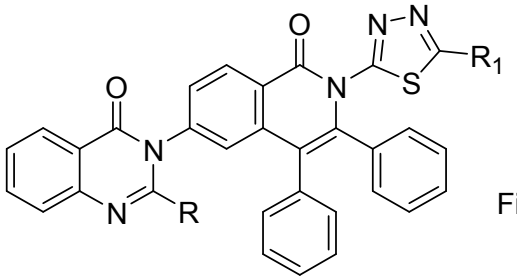


Fig 13

R1 = diff. Aryl groups, R = H.

Synthesis and antifungal activity of some novel 6-bromo-2-methyl/phenyl-3-(sulphonamido) quinazolin-4(3H)-ones (Fig 14) were evaluated by Selvam et al. (2004).

Same as Paneersalvam et al. (2003) also synthesized a series of 2-methylquinazolin-4(3H)-ones (Fig 15) . The compounds were also screened for their antifungal activity.

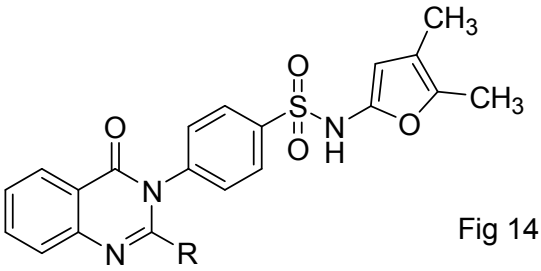
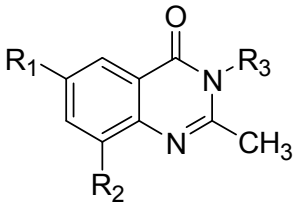


Fig 14

R=CH3, C6H5



R1 =H, Br
R2 =H,Br

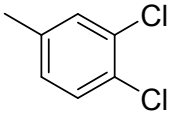
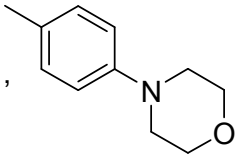
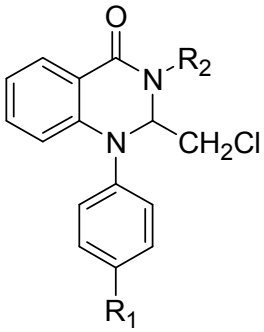
R3 =  , 

Fig 15

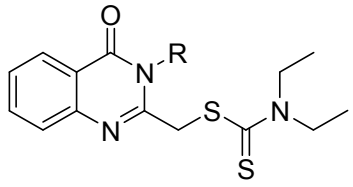
Some new 1-substituted-2-(chloromethyl)-4-(1H)-quinazolinones (Fig 16) were synthesized and screened for their antifungal activity by Gangwal et al. (2001).



R1 =H, NO2, OCH3.
R2 = Substuted Ar

Fig 16

In-vitro antifungal activity aganist fungal strain and synthesis of some analogues of 2-methyl quinazolinones (Fig 17) were reported by Farghaly and Moharram (2002).



R= H, 4-MeC_6H_4, 4-ClC_6H_4 etc.

Figure 17

Significant antifungal activity was observed for new 6,8-dichloro-2-phenyl-4-(3H)-quinazolinone moieties (Fig 18) by Ibrahim (1998).

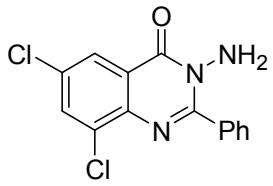
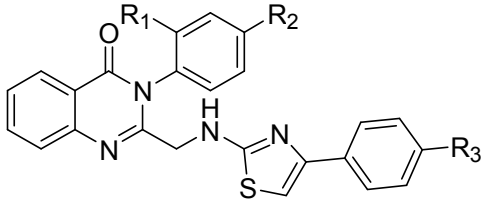


Figure 18

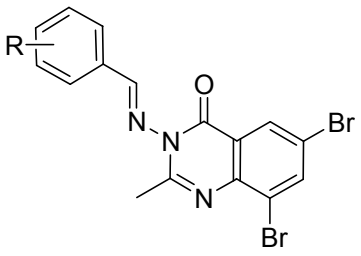
A series of 3-aryl-2-(4′-arylthiazol-2′-yl aminomethyl)-quinazol in-4(3H)-ones (Fig 19) have been elicited for their impressive fungicidal activities by Pattanaik et al. (1998).



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

Figure 19

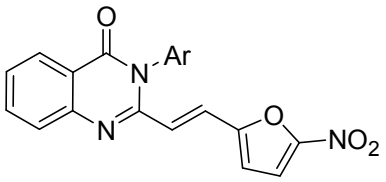
New 2,3- and 2,4-disubstituted quinazoline (Fig 20) synthesized by Mahr et al. (2011) derivatives as potential antibacterial and antifungal agents .



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

Figure 20

3-Aryl-2-[(5-nitro-2-furfuryl)vinyl]quinazolin-4-ones (Fig 21) were prepared and screened for fungicidal activity by Shivananda and Shivarama . (2011).



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

Figure 21

Pharmacological screening of some quinazolinones (Fig 22) synthesized by Bekhit et al. (1995) displayed activity against various fungal species.

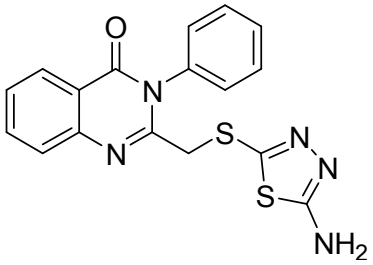


Figure 22

Singh et al. (1994) synthesized 6-(4´-substituted-benzylidene-2´-methyl /phenyl-5´-imidazolinon-1´-yl)-2-methyl-4(3H)-quinazolinone (Fig 23)and assessed the compounds for their antifungal activity against Aspergillus niger.

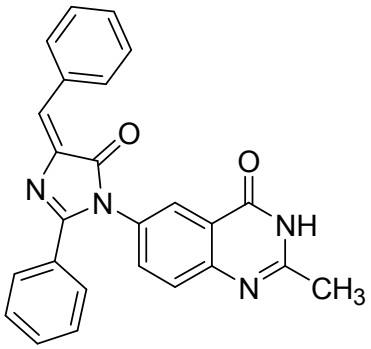
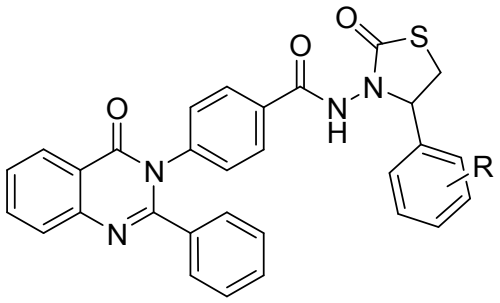


Figure 23

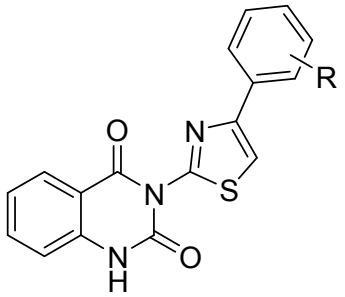
Potent antifungal activity in some newer quinazolinones (Fig 24) containing thiazolidinone moiety was reported by Trivedi et al. (1993).



R= Cl, OCH_3, H etc.

Figure 24

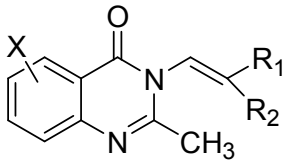
3-(4'-aryl-2'-thiazolyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazolinones (Fig 25) as promising antifungal agents were synthesized by Khan and Rastogi (1993).



R= 4-Br, 2-Cl, H, 4-Me etc.

Figure 25

Some Schiff bases of 3-amino-2-methylquinazolin-4(3H)-ones (Fig 26) were prepared and evaluated for their antifungal activity by Mishra et al. (1991).



X= H, Br
R_1= H, Me, Ph etc.
R_2= Ph, 2-$OCH_3C_6H_4$ etc.

Figure 26

2-(4-aryl-2-pyrazolin-3-yl)-3-aryl-4(3H)-quinazolinones (Fig 27) have been prepared by cycloaddition of diazomethane by Reddy et al 1991. Their structures have been elucidated on the basis of elemental analysis and spectral data. Some of these compounds have been found to exhibit good antifungal activity.

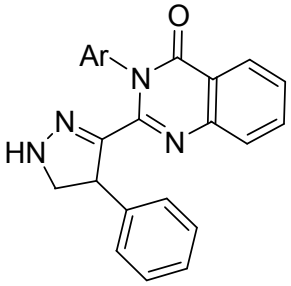


Figure 27

A condensation of four defferent 3-formylchromones with 2-methyl/phenyl-3-amino-4(3H)-quinazolinone and their dibromo analogs has resulted in twelve new compounds which have been characterized as their respective 3-[N-(4-oxo-2-methyl/phenyl-3-quinazolinyl)-formimidoyl]-chromones (Fig 28), base on their spectro-analytical properties. These compounds have been investigated as antifungal agent by Achaiah et al 1991.

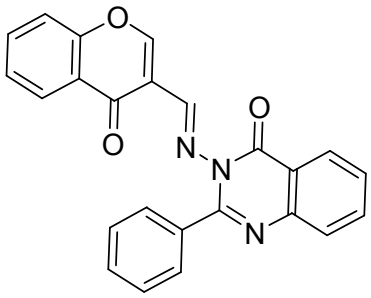


Figure 28

CONCLUSION

The literature reveals that the newly synthesized compounds exhibited good antifungal activity against *Candida albicans, aspergilles niger, aspergillus Clavatus, Aspergillus fumigatus, Aspergillus Parasiticus* at various concentrations. Recently several scientists have been elucidated that substitution at 2 & 3 positions markedly modulate antifungal activity. Several workers have also synthesized 2, 3-substituted quinazolenone containing different heterosystems which were found to posses potent anti fungal activities. By the present scenario it can be concluded that substituted quinazolenones have a great potential which remain to be disclosed till date.

REFERENCE

1. Achaial G, Reddy V M, Reddy V Malla. Synthesis and biological activities of 3-[n-(4-oxo-2-substituted-3-quinazolinyl) formimidoyl] chromones. Indian J Pharm. Sci., 53, 253-255, (1991).
2. Anjani K. Tiwari, Vinay Kumar Singh, Aruna Bajpai, Gauri Shukla, Sweta Singh, Anil K. Mishra. Synthesis and biological properties of 4-(3*H*)-quinazolone

derivatives European Journal of Medicinal Chemistry, 42 (9), 1234-1238 (2007).

3. Bekhit, A.A. Synthesis and Antimicrobial Evaluation of Some Quinazolinone Derivatives Bull. Pharm. Sci. Assiut Univ. 18, 107-114 , (1995).
4. Bekhit AA, Habib NS, El-Din A, Bekhit A.. Synthesis and antimicrobial evaluation of chalcone and syndrome derivatives of 4-(3H)-quinazolinone. Boll Chim Farm. 140(5), 297-301,(2001).
5. Bhusare, S.R., Shinde, A.B., Pawar, R.P., and Vibhute, Y.B. Synthesis And Antimicrobial Activity Of Heterocyclic Schiff Bases, 4-Thiazolidinones And 2-Azetidinones. Indian J. Pharm. Sci., 66, 228-231, (2004).
6. Moustafa MA, Eisa H M. Synthesis and antimicrobial activity of 3-(substituted-phenyl)-sydnones.Arch Pharm (Weinheim). 325(7), 397-401, (1992).
7. Deshmuhk M B, Patil S, Patil S S and Jadhav S D. Synthesis and antimicrobial screening of pyrazolo-3-aryl quinazolin-4(3h)ones. Indian J Pharm. Sci., 72 (4), 500-504 (2010).
8. Nagwa M. Abdel Gawad, Hanan Hanna Georgey, Riham M. Youssef and Nehad A. El Sayed . Design, synthesis, and anticonvulsant activity of novel quinazolinone analogues Medicinal Chemistry Research, 20 (8), 1280-1286, (2011).
9. Farghaly, A.O., and Moharram, A.M. Thioglycolic acid and pyrazole derivatives of 4(3H)-quinazolinone: synthesis and antimicrobial evaluation Boll. Chim. Farm., 138, 280-289, (2002).
10. Gangwal, N.A., Kothawade,U.R., Galande, A.D., Pharande, D.S., and Dhake, A.S. Synthesis of 1-substituted-2-2cholromethyl-4-(1H)-quinazolinones as antimicrobial agents . Indian J. Heterocycl. Chem., 10, 291-294, (2001).
11. Gaurav Grover, Suvarna G. Kini. Synthesis and evaluation of new quinazolone derivatives of nalidixic acid as potential antibacterial and antifungal agents European Journal of Medicinal Chemistry, 41(2), 256-262, (2006).
12. Ibrahim KM Synthesis and antimicrobial evaluation of certain new 6,8-dichloro-2-phenyl-4(3H)quinazolinone derivatives. Egypt J Pharm Sci 39, 519-531, (1998).
13. Khan, R.H., and Rastogi, R.C. Synthesis and antimicrobial activity of 3-(4'-aryl-2'-thiazole)-2,4-dioxo-1,2,3,4-tetra hydroquinazolines and 2-(4'-aryl-2'-Tthiazolylamino)-4-oxo-4H-3, 1-benzoxazine from methyl N-(4-arylL-2-thiazolyl)dithiocarbamates. Indian J. Chem., 32, 595-598, (1993).
14. Matysiak J and Malinski Z. 2-(2,4-dihydroxyphenyl)-1,3,4-thiadiazole analogues: Antifungal activity in vitro against *Candida* species. Russian J Bioorganic Chem. 33 (6), 594-601. (2007).
15. Soroush Sardari, Yoki Mori, Kiyoshi Horita, Ronald G Micetich, Sansei Nishibe, Mohsen Daneshtalab. Synthesis and antifungal activity of coumarins and angular furanocoumarins Bioorganic & Medicinal Chemistry 7(9), 1933–1940, (1999).
16. Mahr A. El-Hashash1, Dalal B. Guirguis1 and Yaser A. El-Badry. Synthesis and evaluation of new 2,3- and 2,4-disubstituted quinazoline derivatives as potential antibacterial and antifungal agents. Der Pharma Chemica, 3 (6), 147-159, (2011).
17. Mani C. P, Yakaiah T, G. Gayatri, Pranay K. K, Narsaiah B, Murthy U.S.N., Raghu A. R R. Click chemistry: Studies on the synthesis of novel fluorous tagged triazol-4-yl substituted quinazoline derivatives and their biological evaluation – Theoretical and experimental European Journal of Medicinal Chemistry, 45(1), 78-84, (2011).
18. Mishra, P., Jain, S.K., Jain, S. Synthesis of Some New Quinazolin-4(3H)-ones as Possible Antimicrobial Agents.J. Indian Chem. Soc., 74, 816-817, (1991).

19. Mosaad S. Mohamed, Mohsen M. Kamel, Emad M.M. Kassem, Nageh Abotaleb, Sherein I. Abd El-moez, Marwa F. Ahmed. Novel 6,8-dibromo-4(3*H*)quinazolinone derivatives of anti-bacterial and anti-fungal activities European Journal of Medicinal Chemistry, 45 (8), 3311-3319, (2010).
20. Omar, A.M.E., El-Dine, S.A.S., Labouta, I.M., and El-Tombary, A.A. Synthesis and evaluation for Antimicrobial and antihistaminic properties of new thiosemicarbazide and triazole derivatives of triazolo [4,3-a] quinazolin-5 [H] - onesAlexandria J. Pharm. Sci., 5, 213-215, (1991).
21. Palani V. and Vijay S. T. Design and synthesis of Quinazolinone, Benzothiazole derivatives bearing guanidinopropanoic acid moiety and their Schiff bases as cytotoxic and antimicrobial agents . Arabian J Chem. 2011 (artical In Press) doi: 10.1016/j. arabjc.2011.09.004.
22. Pandey V.K., Pathak, L.P., and Mishra, S.K. Synthesis and characterisation of isoquinolinyl quinazolines and a study of their antiviral and antifungal activities Indian J. Chem., 44, 1940-1944, (2005).
23. Pandey, V.K., Gupta, V.D., Upadhyay, M., Upadhyay, M., Singh, V.K., and Tandon, M. Synthesis, characterization and biological activity of 1,3,4-substituted 2-azetidinonesIndian J. Chem., 44, 158-162, (2005).
24. Paneerselvam, P., Pradeepchandran, R.V., and Sridhar, S.K. Synthesis, Characterization And Biological Activities Of Novel 2-Methyl-Quinazolin-4(3H)-Ones Indian J. Pharm. Sci., 65, 268-273, (2003).
25. Patel, R.B., Desai, P.S., Desai, K.R., and Chikhalia. Synthesis of pyrimidine based thiazolidinones and azetidinones: Antimicrobial and antitubercular agents. Indian J. Chem., 45, 773-778, (2006).
26. Pattanaik,J. M., Pattanaik,M., and Bhatta, D. Synthesis and Fungicidal Activity of 3-Aryl-2-(4′-aryl thiazol-2′-ylaminomethyl)quinazol-4(3H)-ones. Indian J. Chem., 37, 1304-1306, (1998).
27. Perumal P, Bilal A R, Dontireddy R S R, Natesh R K. Synthesis and anti-microbial screening of some Schiff bases of 3-amino-6,8-dibromo-2-phenylquinazolin-4(3*H*)-ones European Journal of Medicinal Chemistry, 44 (5), 2328-2333, (2009).
28. Popat, K.H., Kachhadia, V.V., Nimavat, K.S., and Joshi, H.S. Synthesis of Some New Cyanopyrans and Cyanopyridines and Their Biological Activities. J. Indian Chem. Soc., 157-159, (2004).
29. Priya M G R. , Zulykama Y., Girija K., Murugesh and Perumal P L. Synthesis of 4-(3*H*)-quinazolinones by microwave assisted tandem reaction and evaluation of their antibacterial and antifungal activities. Indian J of Chemistry. 50 ,98-102, (2011).
30. Raj, M.P.P., and Rao, J.T. Synthesis of Some Difuralidenehydrazide Derivatives of 1,4-Dihydropyridine as Possible Antifungals and Insecticides. Asian J. Chem., 15, 492-496, (2003).
31. Rajanarendar, E., Karunakar, D., and Srinivas, M. Synthesis and bioactivity of isoxazolyl thiazoles, isoxazolyl thiazolyl chromen-2-ones, isoxazolyl thiazinanes and isoxazolyl thiazolidinones Indian J. Chem., 43, 643-648, (2004).
32. Rajput C. S.,Sharma S., Kumar A.; **S**ynthesis Of 3-Substituted Quinazolinones As Antifungal Agents Organic Chemistry An Indian J., 7(1), (2011).
33. Rajput C. S., Kumar S and Kumar A. Synthesis and antifungal activity of newer substituted Quinazolinones; International J. Chem tech Research, 2(3), 1653-1660, (2010).
34. Reddy A M, Reddy R R, Reddy VM, Reddy A Malla, Reddy RR, Reddy V Malla. Synthesis and antifungal activity of 2-(4-aryl-2-pyrazolin-3-yl)-3-aryl-4 (3h)-

quinazolinones. Indian J Pharm. Sci. 53, 229-232, (1991).
35. Sarvesh K. P, Abhishek S, Ashutosh S, Nizamuddin. Antimicrobial studies of some novel quinazolinones fused with [1,2,4]-triazole, [1,2,4]-triazine and [1,2,4,5]-tetrazine rings European Journal of Medicinal Chemistry, 44(3), 1188-1197, (2009).
36. Selvam ,P., Vanitha, K., Chandramohan, M., and Clerco, E.D.E. Synthesis And Antimicrobial Activity Of Some Novel 6-Bromo-2-Methyl/phenyl-3-(Sulphonamido) quinazolin-4(3H)- Ones . Indian J. Pharm. Sci., 66, 82-86, (2004).
37. Singh, S., Dave, U., and Parikh, A.R. Studies on Imidazolinones: Synthesis and Antimicrobial Activity of 6-(4′-Substituted-benzylidene-2′-methyl/phenyl-5′-imidazolinon-1′-yl)-2- methyl-4(3H)-quinazolinone. J. Indian Chem. Soc., 71, 159-160, (1994).
38. Shivananda M K and Shivarama B. H. Antifungal activity studies of some quinazolinone derivatives J. Chem. Pharm. Res., 3(3):83-86, (2011).
39. Singh, T., Sharma, S., Srivastava, V.K., and Kumar, A. Synthesis and Biological Evaluation of Some Pyrazolinylpyridines and Pyrazolylpyridines Arch. Pharm. Chem. Life Sci., 339, 24-31, (2006).
40. Trivedi, P.B., Undavia, N.K., Dave, A.M., Bhatt, K.N., and Desai, N.C. Synthesis and Antimicrobial Activity of Some Heterocyclic CompoundsIndian J. Chem., 32, 497-500, (1993).
41. Vasoya, S.L., Patel, M.R., Dobaria, S.V., and Joshi, H.S. Facile. Facile synthesis of some new azetidinones and acetyl oxadiazoles bearing benzo[b]thiophene nucleus as a potent biological active agent. Indian J. Chem., 44, 405-409, (2005).
42. Yelamaggad, C.V., Hiremath, U.S., and Badami, B.V. Reactions of 4-(4-Thiazolyl)sydnones: Synthesis of 4-(2-(2,5- Dimethylpyrrol-1-yl)thiazol-4-yl)-3-arylsydnones Indian J. Chem., 34, 346-347, (1995).