Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2015, 7(5):1279-1287

Review Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Potential antimicrobial activities of quinazolinone derivatives

Gollapalli Naga Raju*, Karumudi Bhavya Sai, Vallampatla Resshma, Nallapu Sudarshini, Peruru Lakshmi Sowmya, Yekula Nalini and Rama Rao Nadendla

Department of Pharmaceutical Analysis, Chalapathi Institute of Pharmaceutical Sciences, Guntur, India

---

ABSTRACT

Heterocyclic compounds possess diverse biological properties that have lead to intense study and research of these compounds. One of these compounds is Quinazolinone which has been found to exhibit various pharmacological activities. Quinazolinone having heterocyclic nucleus is a novel molecule which attract the chemist to search a new therapeutic molecule. The present review article covers various derivatives of different Quinazolinone and their substitutions with antimicrobial activities.

Keywords: Quinazolinone, Antimicrobial, Antibacterial, Antifungal

---

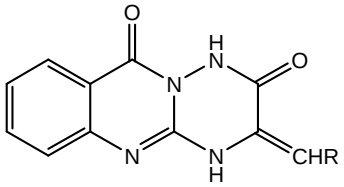
INTRODUCTION

Heterocyclic chemistry is a chemistry involving the heterocyclic compounds which contain atoms of at least two different elements as number of ring. The heterocyclic may be inorganic, though the compound has carbon atoms in the ring, the word hetero means different from carbon and hydrogen. Nitrogen containing heterocyclic compounds plays an important role in medicinal chemistry. Quinazolinone consists of two fused benzene and pyrimidinone ring. Quinazolinones are a large class of active chemical compounds exhibiting a broad spectrum of biological activities in animals as well as in humans. Literature studies on quinazolinones have shown that these derivatives possess a wide variety of biological activities such as antioxidant[1], antifungal[2], antibacterial[3], anticonvulsant[4], antiinflammatory[5], antihyperlipidemic[6], anticancer[7], antimalarial[8], antispasmodial[9] analgesic[10], antiviral[11], antitubercular[12] and antimicrobial[13] activities.

Quinazolinones are classes of fused heterocycles that are of considerable interest because of the diverse range of their biological properties. Quinazolinones will be classified into the following five categories, based on the substitution patterns of the ring system; they are 2-Substituted-4[3H]-quinazolinones, 3-Substituted-4[3H]-quinazolinones, 4-Substituted-quinazolines, 2,3-Disubstituted-4[3H]-quinazolinones and 2,4-Disubstituted-4[3H]-quinazolinones. Depending upon the position of the keto group, these compounds may be classified into three types. They are 2[1H] quinazolinones, 4[3H] quinazolinones and 2, 4[1H, 3H] quinazolindione.

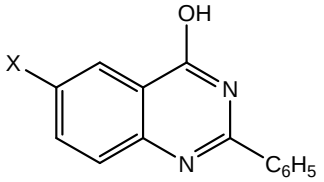
Quinazolinone is one of the most important heterocyclic compound, weak base, having varied biological activities and still of great scientific interest now a days. They are widely found in bioorganic and medicinal chemistry with application in drug discovery. This review was focused on the Quinazolinones and its different derivatives that posses antimicrobial activities.

Antimicrobial activity:
Break L.M. and Mosselhi M.A.N. et al carried out the Synthesis, Structure and Antimicrobial Activity of new 3- and 2-Arylmethyl and arylacyl-3H[1,2,4]triazino[3,2-b]-quinazoline-2,6(1H)diones. The products obtained are tested for antimicrobial activity and reported [14].



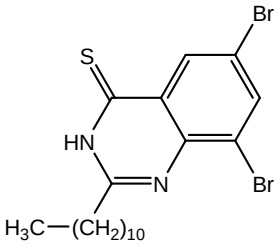
R = COC_6H_5
= COC_6H_5-OCH_3-4
= COC_6H_5-Br-4

A novel series of 4, 6-substituted quinazoline derivatives have been synthesized by Sucheta et al. All the derivatives are screened for anti-microbial activity. Promising compounds which showed activity have been identified [15].

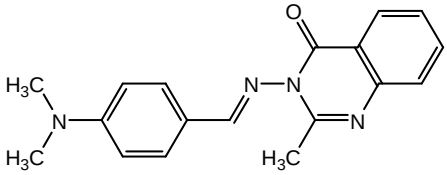


X
QZ-1 CH_3
QZ-2 HBr
QZ-3 CH_3I
QZ-4 OCH_3

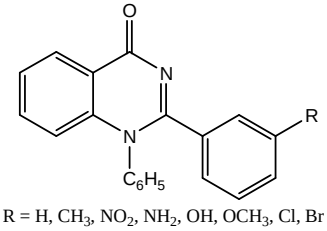
A.A. Abdalha et al are carried out the study of Antimicrobial Susceptibility of Certain Fungal and Bacterial Strains to Dodecanamide and Quinazolinone Derivatives. The results revealed that majority of the synthesized compounds showed varying degrees of inhibition against the tested microorganisms [16].



Ahmed A. H. Al-Amiery et al, Synthesized some of the Novel quinazolinone derivatives. All synthesized compounds were tested *in-vitro* against a number of microorganisms (*Staphylococcus aurous, E.coli, Proteus vulgaris, Pseudomonas, and Klebsiella*) and two fungal *Aspergillus niger* and *Candida albicans* in order to assess their antimicrobial properties [17].

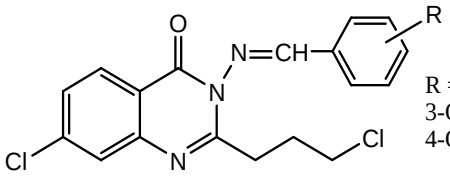


Kunwar Pratap Singh et al Synthesized 1, 2 Di-Substituted Quinazolinone Derivatives. These compounds are also screened for biological activity like anti-microbial activity using standard disk method by measuring inhibition of zone. Ceftriaxone was used as standard drug. The synthesized compound was shown to good anti-microbial activity as compared with standard [18].



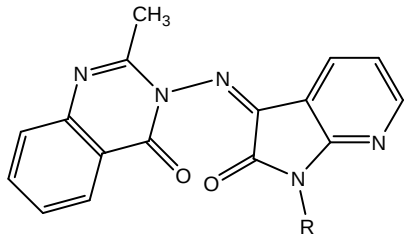
R = H, CH_3, NO_2, NH_2, OH, OCH_3, Cl, Br

A series of 7-chloro-2-(3-chloropropyl)-3-[(substitutedbenzylidene) amino]quinazolin-4-(3*H*)- ones carrying different aromatic moieties were prepared and tested for their activity against certain strains of Gram negative bacteria, Gram positive bacteria and pathogenic Fungi by Snehal Lokhandwala et al. The results revealed that some of synthesized compounds displayed marked activity against some of the tested microorganisms [19].



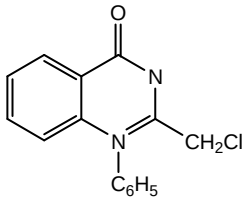
R = 4-OCH_3, 3-Cl, 3-Br, H,2-NO_2, 3-OC_6H_5, 4-OH-3-OC_2H_5, 4-OH-3-OCH_3, 4-OH-3,5-$(CH_3)_2$

Karumanchi Anupama Devi et al synthesized some of the Quinazolinones Derivatives. Newly synthesized compounds were screened for antibacterial activity against gram positive bacteria Bacillus subtilis, Staphylococcus aureus, Streptococcus pneumonia and gram negative bacteria Escherichia coli, Proteus vulgaris, Klebsiella pneumoniae, Pseudomonas aeruginosa and four fungus Aspergillus niger, Aspergillus flavus, Candida albicans and Fusarium oxysporium by using disc diffusion method at 10 µg/disc. Solutions of Ciprofloxacin and Fluconazole were used as standard antibacterial and antifungal drugs respectively [20].

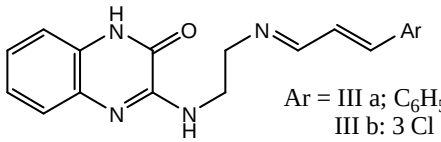


R = CH_3, C_2H_5, C_3H_7, C_6H_{13}

Some of the Novel Quinazolinone Derivatives were synthesized by the Ratnakar Singh et al. These compounds were also screened for various biological activities like anti-microbial activity by standard methods. The synthesized compounds have shown moderate to good anti-microbial activity and some synthesized compound has shown significant as compared with standard [21].

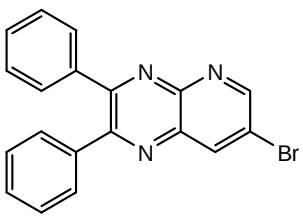


Some of the 3-substituted [(phenyl) methylidene] amino}ethyl)amino]quinoxalin-2(1H)-one have been synthesized by the Ratnadeep V. Ghadage et al. All the final derivatives were evaluated for antimicrobial activity *in-vitro* by using Disc diffusion method. It was found that all the selected compounds exhibit wide antimicrobial activity and that compound IIId had a broad spectrum of activity [22].



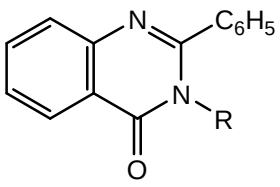
Ar = III a; C_6H_5-CH_2CH=CH CHO
III b: 3 Cl - C_6H_4CHO
III c: $(CH_3)_2N$-C_6H_4CHO
III d: 3, 4 Cl^- C_6H_3 CHO
III e: 2 OH $C_{12}H_8CHO$

Yellajyosula Lakshmi Narasimha Murthy et al synthesized the 2,3-Diphenyl Quinoxaline 1,4-di-*N*-oxide Derivatives and investigate the antimicrobial activities. The study would be a fruitful matrix for the development of 2,3-diphenyl quinoxaline 1,4-di-*N*-Oxide derivatives for further biological evaluation [23].



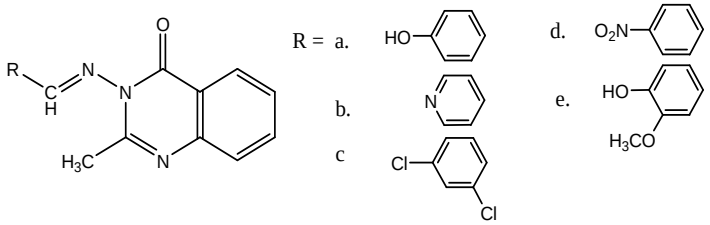
A.U. Kale et al synthesized some of the 2, 3-Disubstituted Quinazoline-4(3h)-Ones. These compounds were tested for *in-vitro* antibacterial activity against *Escherichia coli*, *Staphylococcus aureus* and antifungal activity against

Aspergillus niger, *Candida albicans* by standard methods. These synthesized compounds have been shown moderate to good antibacterial as well as antifungal activity when compared with standard [24].



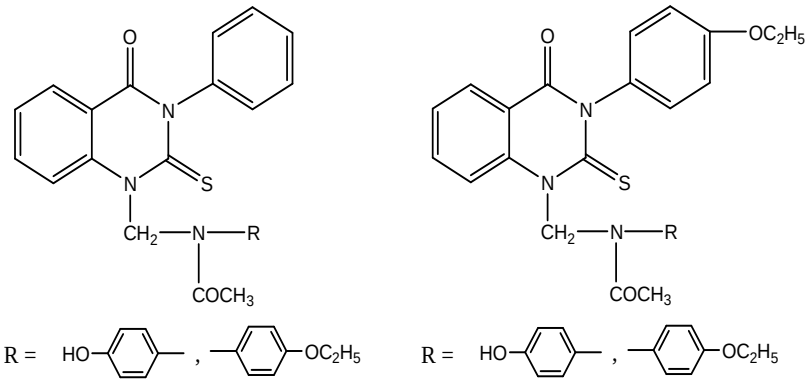
R = $A_{1.}$ Aniline
$A_{2.}$ Thiourea
$A_{3.}$ 4-aminobenzenesulfonamide
$A_{4.}$ Urea
$A_{5.}$ Acetamide
$A_{6.}$ 4-Fluoroaniline

A series of new Schiff Bases Containing 4(3H)-Quinazolinone Ring System were prepared by Hosakere. D. Revanasiddappa et al. The compounds were also evaluated for their antimicrobial, anthelmintic and antioxidant activities. The results suggest that the compounds possess broad spectrum of *in vitro* antimicrobial activity. An anthelmintic result reveals that the compound 3c is potentially active against earth worms. Antioxidant results obtained in the present study indicate that few of the synthesized compounds show moderate to better scavenging activity [25].

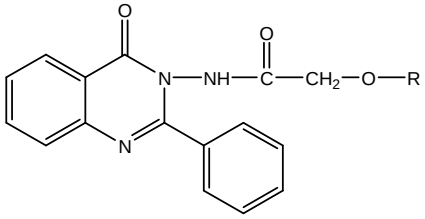


A series of ten novel derivatives of 3-substituted-2-thioxoquinazolin-4(3H)-ones have been synthesized by A. Rajasekaran et al. The synthesized compounds were subjected to antimicrobial screening by cup plate method and broth dilution method. The newly synthesized compounds were screened for their anticonvulsant activity by the Maximal Electroshock (MES) induced seizures method, wherein electroshocks were applied via corneal electrodes using phenytoin as a reference drug[26]

.

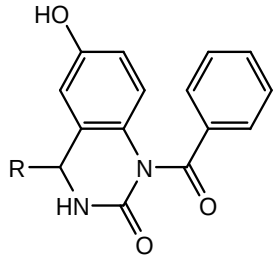


Quinazolinone derivatives were synthesized by Deepti Kohli et al. All the newly synthesized quinazolinone derivatives were evaluated for their antibacterial activity by cup plate method by measuring inhibition zone. Ampicillin was used as standard drug[27].



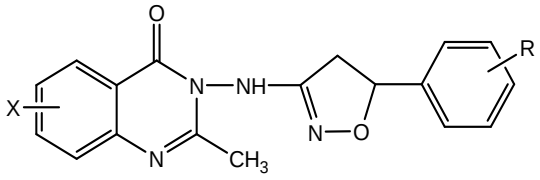
R = DK^{-1} C_6H_5
DK^{-2} 4-$NO_{2.}C_6H_4$
DK^{-3} 4-Cl.C_6H_4
DK^{-4} 2,6-Cl.C_6H_3
DK^{-5} 2-$COOCH_{3.}C_6H_4$
DK^{-6} 4-Cl.3-$CH_{3.}C_6H_3$
DK^{-7} 2-$OCH_{3.4}$-$CH_{2.}CH{=}CH_{2.}C_6H_3$

Suba Geetha A. et al synthesized the some of the 1-Benzoyl-6- Hydroxy-3,4 Dihydro Quinazoline Derivatives. The entire synthesized compounds have been evaluated for their antimicrobial activity [28].



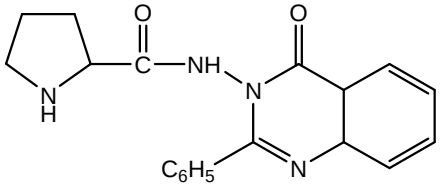
R = 2-aminophenyl, 3-chloro-4-nitrophenyl, 2-chlorophenyl, 4-methoxyphenyl, 2-nitrophenyl, 4-phenyl

Maninder Minu et al carried out the study of QSAR modeling on Quinazolinonyl Pyrazolines and Quinazolinoyl Isoxazolines as Anticonvulsant Agents. This study was performed on compounds having quinazolinonyl ring substituted at position 3 with pyrazoline and isoxazoline moieties to find out the structural requirements for anticonvulsant activity [29].

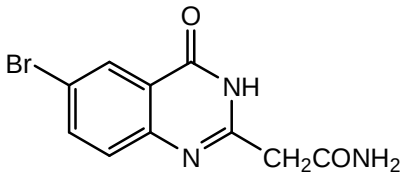


5a	H	H
5b	p-OCH_3	H
5c	p-OH	H
5d	p-$N(CH_3)$	H
5e	m-OCH_3,p-OH	H
5f	H	6-Br
5g	p-OCH_3	6-Br
5h	p-OH	6-Br
5i	p-$N(CH_3)_2$	6-Br
5j	m-OCH_3,p-OH	6-Br

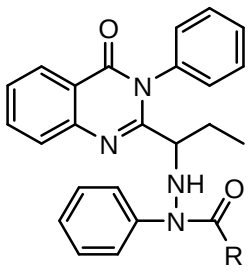
Manish Chaudhari et al synthsized some of the Novel Quinazoline Derivatives and screened for the Anticancer and Anti-Microbial activities [30].



Mona A. Mohamed et al carried out the Biological Evaluation and Molecular Docking of Substituted Quinazolinones. Quinazolinone derivatives possess anti-bacterial activities, especially against the Gram positive strains, and anti-fungal strains through their interaction with the cell wall and DNA structures [31].

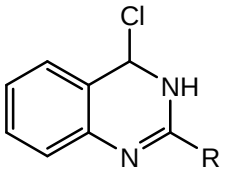


Some new 2,3-disubstituted4(3H)-quinazolinone derivatives were synthesized by G.A. Khodarahmi et al. The *in vitro* antibacterial and antifungal tests of new synthesized compounds were performed using MABA method against six strains of bacteria (three Gram positive and three Gram-negative) and three strains of fungi. Cytotoxic activity of the compounds was screened at 1, 10 and 100 μM concentrations against HeLa cells using the MTT colorimetric assay [32].



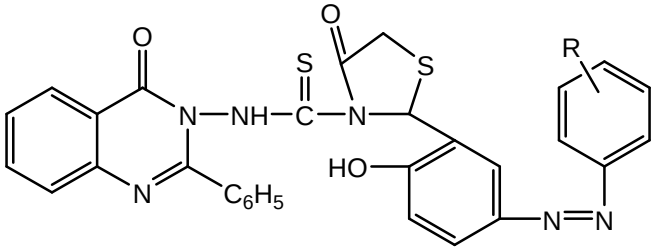
a1: R=Methyl
a2: R=Propyl
a3: R=Phenyl
a4: R=4-Chlorophenyl
a5: R=4-Nitrophenyl
a6: R=3,5-Dinitrophenyl

Chavan B. B. et al synthesized some of the New 4, 6- Disubstituted Quinazoline Derivatives. These derivatives have been a subject of extensive pharmacological evaluation, as well as, toxicological studies for antimicrobial and antifungal activities[33].



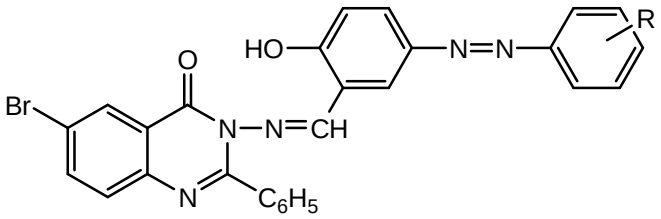
QZ-1 CH_3
QZ-2 HBr
QZ-3 CH_3I
QZ-4 OCH_3

Pushplata Saxena et al synthesized Some of the Novel 2-(2–hydroxy 5- (substitutedphenyldiazyl) -N-[(4-oxo -2-phenylquinazoline 3(*4H)*–yl)]-4-oxo 1,3 thiazolidine-1-carbothioamide. The antimicrobial activities of the synthesized compounds were evaluated by screening on different human pathogens using the disc diffusion assay [34].



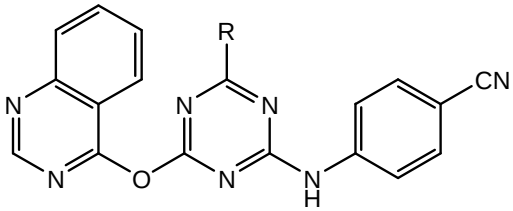
R = -H, m -NO_2, p - NO_2, m - OCH_3, p - OCH_3, p -Cl

Some new biological active 6-bromo-3-({5[3, 4-substituted) diazenyl]-2-hydroxybenzylidene} amino-2-benzylquinazoline-4(3H)-one were synthesized by Tiwari et al. The compounds have been evaluated for their *in-vitro* antimicrobial activity against different human pathogens using disc diffusion assay [35].

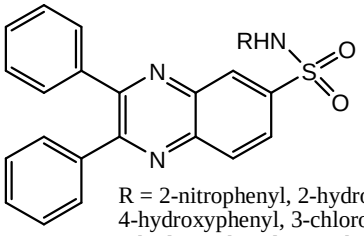


R= H, 4-NO_2, 3-NO_2, 4-OCH_3, 3-OCH_3, 4-Cl, 3-Cl

Two series of 2–(4–cyanophenyl amino)–4–quinoline (quinazoline)–4–yloxy–6–piperazinyl (piperidinyl)–1,3,5–triazines were Synthesized by Kishor H. Chikhalia et al to investigate their antimicrobial and antitubercular action [36].

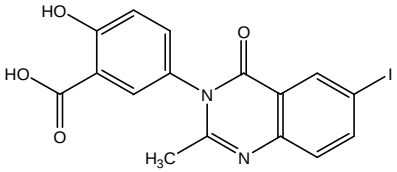


Synthesized novel quinoxaline derivatives, evaluated their antimicrobial activity against various bacterial strains by Rahul Ingle et al. It was found that quinoxaline derivatives of on suitable concentrations have pronounced effect as compared to antibiotic as a reference standard (Azithromycin) present in the market against both the gram positive and gram negative bacteria [37].

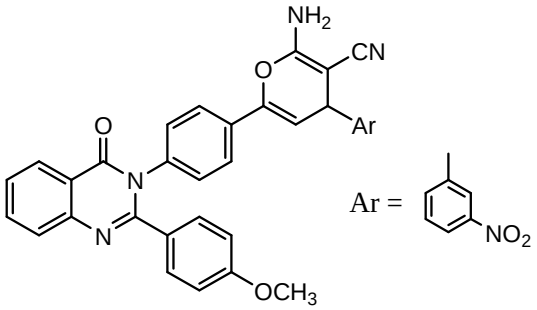


R = 2-nitrophenyl, 2-hydroxyphenyl, 4-chlorophenyl, 4-hydroxyphenyl, 3-chlorophenyl, 3-metoxyphenyl, 3-hydroxyphenyl, 4-methoxyphenyl

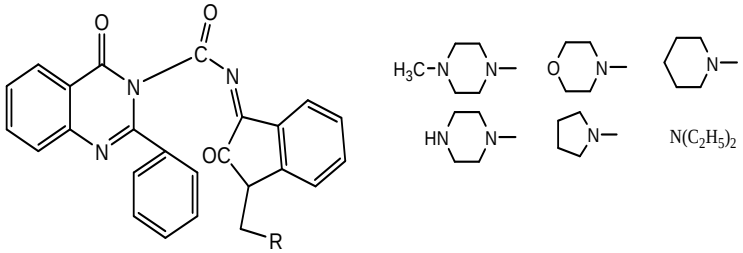
Compound named 2-hydroxy-5-(6-iodo-2-methyl-4-oxoquinazolin-3(4H)-yl) benzoic acid was synthesized by Sachin Chaudhary et al. The newly synthesized cyclopeptide was screened for its antibacterial, antifungal and anthelmintic activities against pathogenic microbes and earthworm species [38].



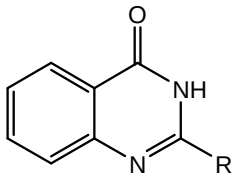
A series of novel derivatives of 2,3-disubstituted quinazolin4(3H)-ones have been synthesized by Firyal Weli Asker et al. These synthesized compounds were evaluated for their antimicrobial activity. The results showed that some of these derivatives have good antimicrobial activities when compared with standard antibiotic [39].



A series of synthons consisting of a heterocyclic core flanked by two basic functionalities isatin and quinazolin-4-(3H)-one were synthesized by Ilango K et al and screened for *in-vitro* antimicrobial activity. Significant antimicrobial activities were observed for some members of the series [40].

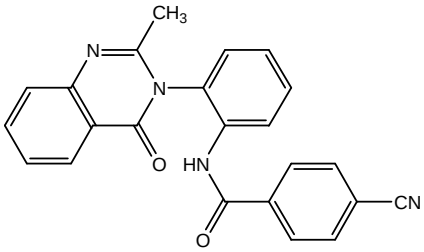


Some New Quinazolin-4(3H)-One derivative was prepared by Nadia Adil Salih. The antibacterial activity of all of the synthesized compounds was also reported. All synthesized compounds have been found to be active against both Gram-positive and Gram-negative bacteria [41].

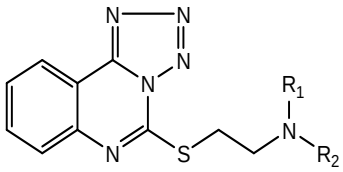


R=NH_2 ; R=CH_3 ; R=Ph ; R=H

Quinazoline-4(3H)-one Derivatives were synthesized by K. Vijayakumar et al. Then antimicrobial and anti-HIV1 activities of the compounds were tested *in-vitro*. It was found that compounds possessed a wide range of anti microbial and anti-HIV1 activity [42].



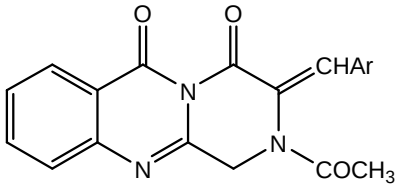
Tetrazolo[1,5-c]quinazoline-5-thione S-Derivatives have been synthesized by L. M. Antypenko et al. The substances were screened for antibacterial and antifungal activities. The substances were screened for their ability to inhibit 60 different human tumor cell lines [43].



R = Me, C_2H_4Ph

$R_1 = R_2$ = H, Me, i-Pr, pip, pyr

2-Acetyl-1,3-diarylidene-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione derivatives were synthesized by the M. A. Zein. The prepared compounds also exhibited antimicrobial activity [44].



Ar = C_6H_5, C_6H_4-CH_3-p, C_6H_4-OCH_3-p

CONCLUSION

From the above literature review concluded that the Quinazolinones and their derivatives have shown a wide spectrum of biological activities. It is a versatile nucleus in the field of medicinal chemistry. Hence this unique molecule must serve as future therapeutic leads of developing various biological agents. The biological profiles of this new generation of Quinazolinones represent much progress with regard to the older compounds.

Acknowledgement
The authors are grateful to Department of Pharmaceutical Analysis, Chalapathi Institute of Pharmaceutical Sciences, Guntur for providing facilities to perform the review work.

REFERENCES

[1] Venakata Ramana Reddy et al, *Int. J. Pharm. Sci. Rev. Res., 29(2),* **2014***; Article No. 01, Pages: 1-4.*
[2] Ahmed Mahal et al, *World Journal of Organic Chemistry*, 2015, *Vol. 3, No. 1, 1-8.*
[3] Nagaraju Gollapalli et al, *AJPAMC, 1(1),* 2013, *48- 53.*
[4] Mohamed F. Zayed, *Journal of Taibah University Medical Sciences (***2014***) 9(2), 104–109*.
[5] D. Channe Gowda et al, *Bioorganic & Medicinal Chemistry Letters* 25 (**2015**) 1072–1077.
[6] AMR Y Esmat et al, *Lipids in Health and Disease* **2005**, 4:22
[7] Nema Rajesh Kumar et al, *Academic Journal of Cancer Research*, **2009**, 2 (2): 73-77.
[8] Mohammed Hussen Bule et al, *IAJPR*, **2015**, Vol 5, Issue 02.
[9] B. Zarranz et al, *Brazilian Journal of Pharmaceutical Sciences*, **2006**, vol. 42.
[10] CH. Rajveer et al, *Int.J.Pharma and Bio Sci*, **2010**,*Vol.1, Issue-3,2010.*
[11] Ratnakar Singh et al, *IJPCBS* **2013**, 3(4), 1269-1275.

[12] Kishor H. Chikhalia et al, *International Journal of Drug Design and Discovery*, **2012**, *Volume* 3, Issue 1, 739-730.
[13] Sucheta et al, *IJPCBS* **2012**, 2(1), 97-103.
[14] L.M.Break and Mosselhi M.A.N. et al, *Res.J.Chem.Sci*, Vol. 2(5), 23-28, May (**2012**).
[15] Sucheta et al, *IJPCBS* **2012**, 2(1), 97-103.
[16] A.A. Abdalha et al, *World Applied Sciences Journal* 24 (3): 312-319, **2013**.
[17] A. H. Ahmed Al-Amiery et al, *Researcher* **2010**;2(4), 82-88.
[18] Kunwar Pratap Singh et al, *IJPCBS* **2013**, 3(4), 1091-1096.
[19] Snehal Lokhandwala et al, *Int. J. Pharm Tech Res.* **2013**,5(3), pp 1126-1131.
[20] Karumanchi Anupama Devi et al, *Int. J. Drug Dev. & Res.*, July-September **2012**, 4 (3): 324-327.
[21] Ratnakar Singh et al, *IJPCBS* **2013**, 3(4), 1269-1275.
[22] Ratnadeep V. Ghadage et al, *International Journal of Experimental Pharmacology*, Vol 2, Issue 1, **2012**, 44-49.
[23] Yellajyosula Lakshmi Narasimha Murthy et al, *RJPBCS* Volume 2 Issue 1, January – March **2011**, 553-560.
[24] A.U. Kale et al, *International Journal of Pharmaceutical and Applied Sciences*/1 (1)/**2010**, 85-90.
[25] Hosakere. D. Revanasiddappa et al, *Int.J. ChemTech Res*.**2010**, 2(2).
[26] A. Rajasekaran et al, *European Review for Medical and Pharmacological Sciences*, **2013**; 17: 95-104.
[27] Deepti Kohli et al, *International Journal of Pharmacy and Pharmaceutical Sciences*, Vol. 1, Issue 1, July-Sep. **2009**.
[28] Suba Geetha A. et al, *International Journal of Biological & Pharmaceutical Research*. **2012**; 3(4): 605-609.
[29] Maninder Minu et al, *J. Adv. Pharm. Edu. & Res*, Jan-Mar **2014**, Vol 4 Issue 1, 59-65.
[30] Manish Chaudhari et al, *International Journal of Science and Research* (IJSR), Volume 3 Issue 11, November **2014**, 3195-3198.
[31] Mona A. Mohamed et al, *Australian Journal of Basic and Applied Sciences*, 7(2): 263-274, **2013**.
[32] G.A. Khodarahmi et al, *RPS* **2012**; 7(3): 151-158.
[33] Chavan B. B. et al, *Asian Journal of Biomedical and Pharmaceutical Sciences*; 4(33) **2014**, 43-46.
[34] Pushplata Saxena et al, *International Journal of Drug Design and Discovery, Volume* 3, *Issue* 1, *January – March* **2012**. 713-717.
[35] Tiwari et al, *Asian J Pharm Clin Res*, Vol 5, Issue 1, **2012**, 98-100.
[36] Kishor H. Chikhalia et al, *International Journal of Drug Design and Discovery*, *Volume* 3, Issue 1, *January – March* **2012**. 739-730.
[37] Rahul Ingle et al, *International Journal of Pharmaceutical Chemistry*, **2014**, 04 (01), 35-38.
[38] Sachin Chaudhary et al, *Asian J Pharm Clin Res*, Vol 5, Issue 4, **2012**,196-200.
[39] Firyal Weli Asker et al, *Chemistry and Materials Research*, Vol.6 No.10, **2014**.
[40] Ilango K et al, *Int. J. Res. Pharm. Sci.* Vol-1, Issue-2, 133-138, **2010**.
[41] Nadia Adil Salih, *Journal of Al-Nahrain University*, Vol.11(2), August, **2008**, pp.16-23.
[42] K. Vijayakumar et al, *Journal of Applied Chemistry*, Volume **2013**, Article ID 387191, 5 pages.
[43] L. M. Antypenko et al, *Sci Pharm.* **2013**; 81: 15–42.
[44] M. A. Zein, *Indian Journal of Research*, Volume: 2, Issue: 4, April **2013**.