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QUINOLINE BASED HETROCYCLIC COMPOUNDS AS ANTI-INFECTIVE AGENTS: A REVIEW

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ABSTRACT - In current scenario recently we all have facing a pandemic which affect our life drastically.but from a long time we are facing many infectious disease which are threat human life at global lavel.various research and efforts have been done for overcome these infectious disease but after some time new drugs became in effective due to developing resistance power in concern micro organism. Quinoline is a very popular and most versatile chemical substance which works on number of disease and use a thereputic agents since long time. New researches shows that many new derivatives of Quinoline work surprisingly on some very mortal disease.

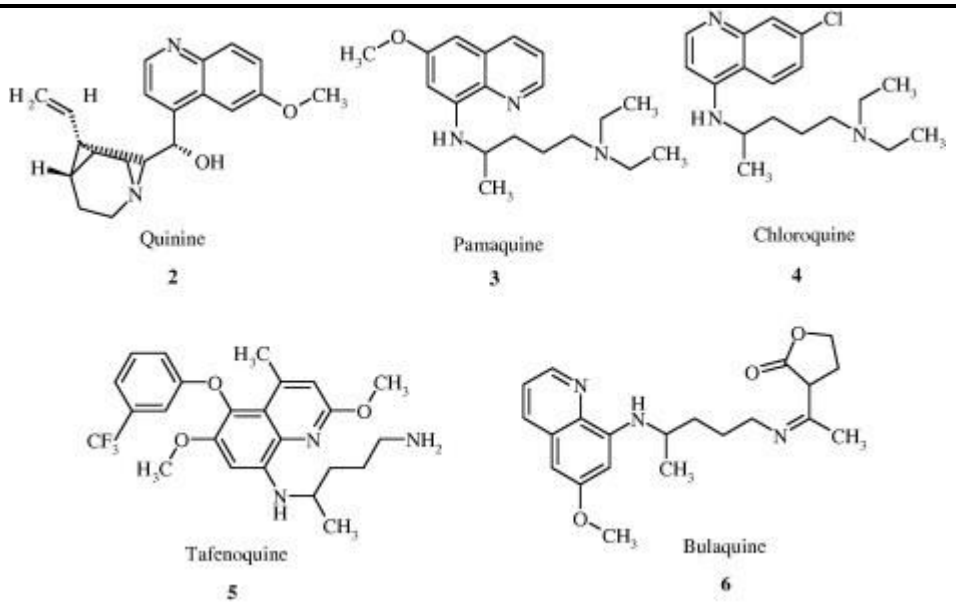
Here we study detailed structure of varios quinoline derivatives which used in cure of many infectious disease.also get information of various activity exhibit by quinoline and their derivatives.new research and development in medicinal field prove that quinoline has numerous potential for working on varios disease like cancer,malaria,micribacterial disease,analgesic ,inflammatory,cardiovascular disfunction,bacterial infection,fungal infection,viral infection,protozoal infection,hypoglycaemic activity,reproductive system etc.so this is necessary to study this hetrocyclic compound for developing number of new very effective versatile drugs.

1. Introduction

Heterocyclic compounds are the cyclic compounds having more than one kind of atom in the ring. Their significance is exhibit from the fact that many of such compounds are of great importance to life occurs in nature. carbohydrates may be classified as oxygen heterocycles (pyranose and Furanose) , whereas the nucleic acid and many amino acids e.g. (pyroline ,hydroxy pyroline and tryptophen) peptides and proteins posses nitrogen containing ring system.

In addition, a wide variety of heterocyclic compounds are prepared primarily by the drug industries. it is therefore thousand of organic chemist Expand there energy in synthesizing novel heterocyclic systems with a view to testing their pharmacological activities. heterocyclic compounds exist in both simple and condensed ring system (mukharjee s.m.et al)

Quinoline nucleus occurs in several natural compounds (Cinchona Alkaloids) and pharmacologically active substances displaying a broad range of biological activity. Quinoline has been found to possess antimalarial, anti-bacterial, antifungal, anthelmintic, cardiotonic, anticonvulsant, anti-inflammatory, and analgesic activity. A few promising compounds [**2**–**6**] with quinoline ring system are given in Fig. 1.

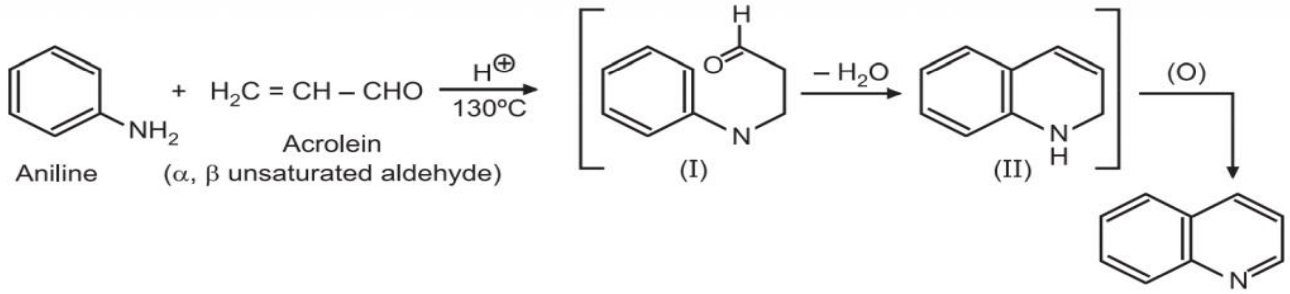


Few promising compounds with quinoline ring system (1)

2. *(a) Some Common Synthetic method -*

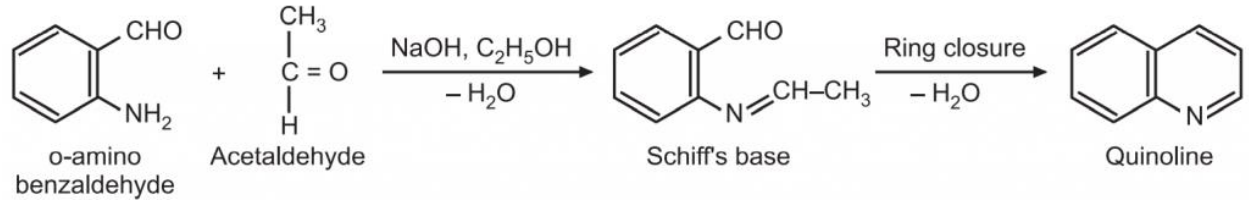
Quinoline formed due to condensation of two cyclic compound of which atleast one would be hetrocyclic compound.in fused hetrocyclics the number system starts from the hetro atom (2) quinoline pka value 4.9 and 5.4 are similar to that of pyridine.some important synthesis methods of quinoline are as follow.(mistri sujay 2021)

A. Skraup synthesis: When aniline, concentrated sulfuric acid, glycerol, and a mild oxidizing agent are heated together, quinoline is formed. The reaction begins when glycerol is first dehydrated by concentrated sulfuric acid to acrolein. Aniline is then added begins to it to produce 1, 2-dihydroquinoline.



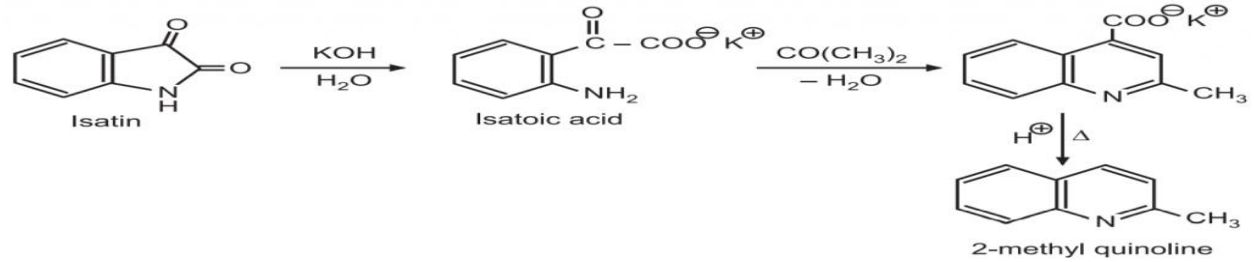
The 1, 2-dihydroquinoline is further oxidized to give quinoline. Aniline adds to acrolein through Michael's addition to give aniline propanal (I). Substituted anilines give quinoline derivatives in which substituents appear in the benzene ring portion.

B. Friedlander synthesis: When o-amino benzaldehyde or o-aminoacetophenone condenses with an aldehyde or ketone (which must contain an active α-methylene group) in alcoholic sodium hydroxide solution, it yields quinoline.

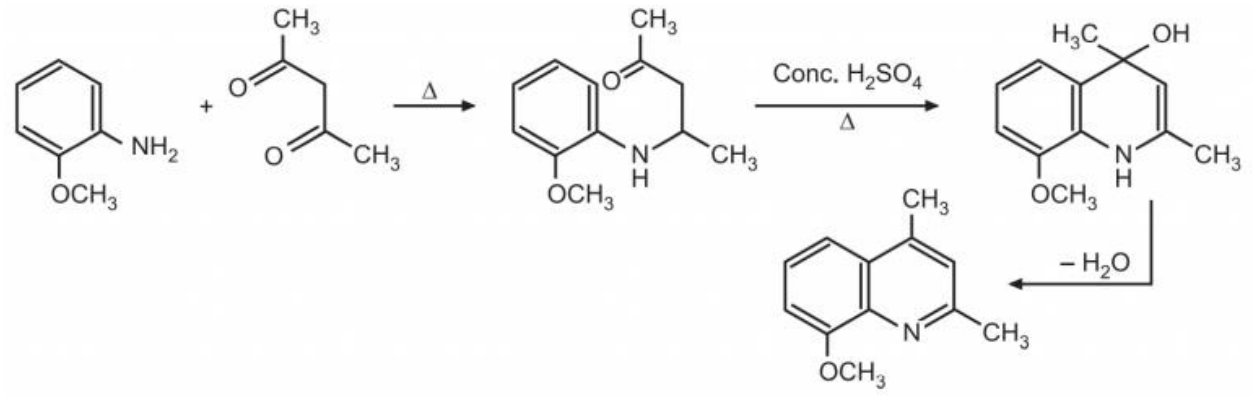


2-substituted quinoline derivatives are usually prepared by this method.

C. Pfitzinger synthesis: In this method, isatin in the presence of a base, is converted to isotonic acid which is condensed with a ketone to give quinoline-4-carboxylic acid. The carboxylic acid group can be removed by pyrolysis with calcium oxide to giv e substituted quinolines.



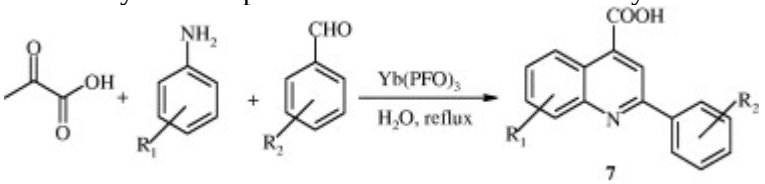
D. Combes synthesis: Condensation of 1, 3-dicarbonyl compound with an arylamine gives a β-amino enone which undergoes cyclization with a loss of water to give quinoline.



2.(b) Synthetic method for differently substituted Quinoline -

A number of established protocols are there for the synthesis of quinoline ring, which can be well modified to prepare a number of differently substituted quinolines.

2-Phenylquinoline-4-carboxylic acid [**7**] has been synthesized by treatment of 2-oxopropionic acid with aniline and benzaldehyde in the presence of rare earth metal catalysts and refluxing in water (Wang et al., 2009a).



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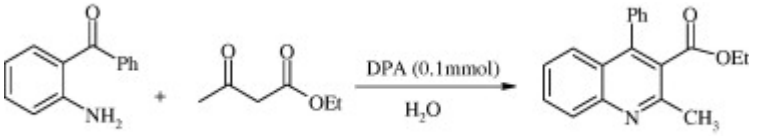

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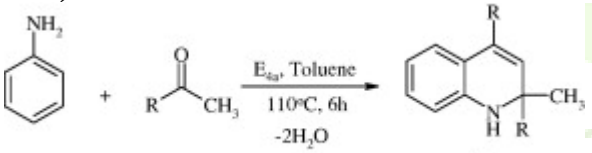
2,4-Diphenyl-2-methyl-1,2 dihydroquinoline [**8**] has been synthesized by using aniline and acetophenone in the presence of a small pore size E_{4a} zeolite catalyst (Hegedus et al., 2007).



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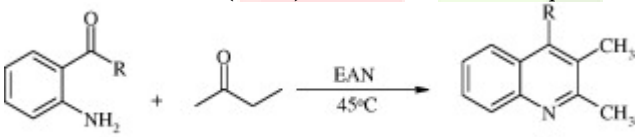
By stirring 2-amino substituted aromatic ketones and carbonyl compounds having a reactive α-methylene group in ethyl ammonium nitrate (EAN) 2,3,4-trisubstituted quinolines [**9**] have been developed (Zhou et al., 2008).



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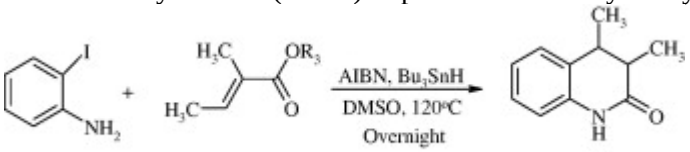
Using 2-aminosubstituted ketone and ketone as reactants poly-substituted quinolines [**10**] have been synthesized in aqueous media and solvent-free conditions in the presence of dodecylphosphonic acid **(DPA) as ca as catalyst (Ghassamipour and Sardarian, 2009).**

3,4-Dihydroquinolin-2-one [**12**] has been developed by treating 2-iodoanilines and ethyl acrylate with Azobisisobutyronitrile (AIBN) in presence of tributyltin hydride (*n*-Bu_3SnH) (Zhou et al., 2009).



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Number of reaction present where quinoline reacts with various of reactants in the presence of specific catalyst and temprature pressure condition and produce many derivatives.

Sixteen new 1,3,5-triazine-quinoline derivatives were designed and evaluated as cholinesterase inhibitors . the structure of 1,3,5-triazine-quinoline derivatives were confirmed by IR,NMR,HRMS and single CrystalL X-RAY Diffraction Experiments cholinesterase inhibitory activity of the synthetic compounds were measured using the colorimetric Ellmans synthesis(51-A)

3 .BIOLOGICAL ACTIVITIES OF QUINOLINE DERIVATIVES-

(A) .Anticancer

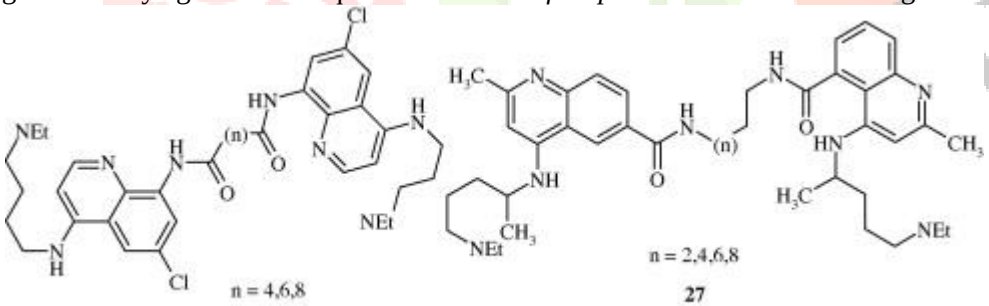
Quinoline derivatives fused with various heterocycleshaves displayed potent anticancer activity targeting different sites like topoisomerase I, telomerase, farnasyl transferase Src tyrosine kinase, protein kinase CK-II etc. Indole fused10H-indolo[3,2-b]quinoline bearing bis-dimethylaminoethyl chain have been synthesized and evaluated for anticanceractivity by Vittorio Caprio *et al.* and compound was found to be act on telomerase with IC50 16M .Intercalation with double stranded DNA is important targetfor cytotoxicity Yuzi Mikata *et al.* reported the synthesisof new derivatives of 2-phenyl quinoline having [(2aminoethyl)aminomethyl] group and compound showed ability to intercalate into double stranded DNA. Dalla Via *et al.* synthesized 1-[4-(3*H*-pyrrolo[3,2-*f*]quinolin-9-ylamino)-phenyl]-ethanone hydrochloride it showed high antiproliferative activity by formingan intercalative complex with DNA and inhibiting DNA topoisomerase II and by blocking the cell cycle in G2/Mphase . *Invitro*antiproliferative activity 8 Baylis–Hillman adducts and their derivatives against a panel of humor

tumor cell lines was studied by Luciana K. Kohn *et al.* and quinoline–phthalide derivative exhibited exhibiteda potent effect on the proliferation of all cell lines. WilliamKemnitzer *et al.*identified novel apoptosis inducerthrough caspase and cell-based high-throughput screening

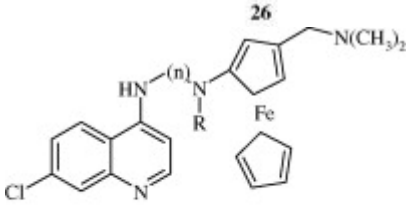
assay and compound 1-(4-(1*H*-imidazol-1-yl)benzoyl)-3-cyanopyrrolo[1,2-*a*]quinoline was found to behighly active in human breast cancer cells T47D, humancolon cancer cells HCT116, and hepatocellular carcinomacancer cells SNU398 cell lines.(53)

(B). Antimalarial

Most important use of the quinoline ring is its antimalarial potential. Bisquinolines [**26**, **27**] developed by Raynes et al. (1996) are found to possess a good degree of antimalarial activity against both chloroquine-resistant and chloroquine-sensitive parasites. Analogues of ferrochloroquine [**28**] were also found to have antimalarial activity by Chibale et al. (2000). In these analogues carbon chain of chloroquine is replaced by hydrophobic ferrocenyl group. Certain 7-chloroquinolinyl thioureas [**29**, **30**] synthesized by Mahajan et al. (2007) are potential antimalarial agents. Modapa et al. (2009) synthesized few ureido-4-quinolinamides [**31**] which showed antimalarial effect at MIC of 0.25 mg/mL against chloroquine-sensitive *Plasmodium falciparum* strain. Chloroquinolyl derivative [**32**] developed by Kovi et al. (2009) also has a potent antimalarial activity at submicromolar levels. Certain 4-aminoquinoline triazines [**33**] synthesized by Kumar et al. (2008) also have antimalarial activity screened against chloroquinine (CQ) sensitive strain 3D7 of *P. falciparum* in an *in vitro* model. Shiraki et al. (2011) developed certain 5-aryl-8-aminoquinolines [**34**] with promising antimalarial activity which had lesser haemolytic activity compared to tafenoquine. Acharya et al. (2008) synthesized and evaluated the antimalarial activity of some pyridine–quinoline hybrids [**35**–**37**] against chloroquine susceptible strain of *P. falciparum*. Singh et al. (2011) developed antimalarial agents with 4-anilinoquinoline ring [**38**]. The compounds showed good activity against chloroquine-sensitive *P. falciparum* strains as well as against rodent malaria parasite *P. yoeii*.



26 **27**



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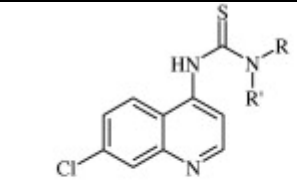
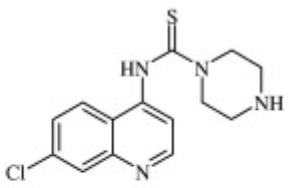


R = $(CH_2)_2OH$, $(CH_2)_3N(Et)_2$, $(CH_2)_3N(Me)_2$, $(CH_2)_2NH_2$

R' = H, C_6H_5, $CH_2C_6H_5$, $COOC_2H_5$

29



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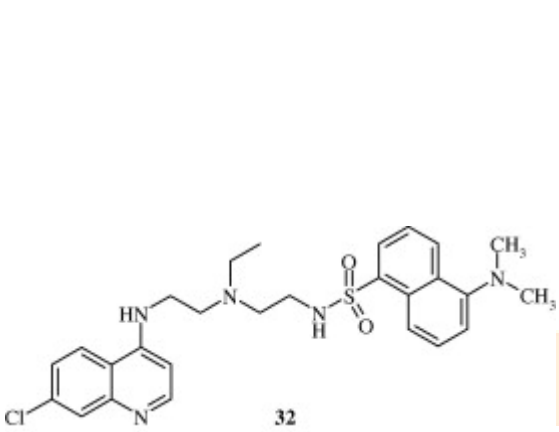

R = Me, Ph, CH_2Cl, 2-ClC_6H_5,3-ClC_6H_5,2-Furyl

R' = F, Cl, Br, CF_3

31

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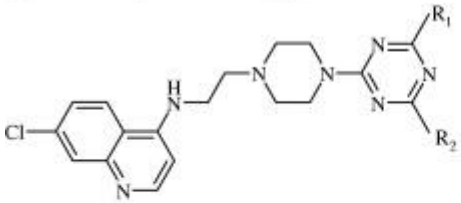
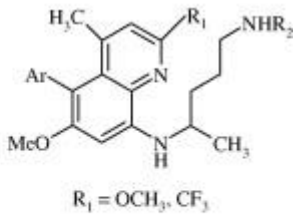


R_1 = *p*-Fluoroaniline, Piperidine

R_2 = Piperidine, Cyclohexylamine

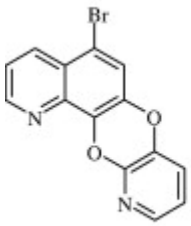
33



R_1 = OCH_3, CF_3

R_2 = H or $C(O)OC(CH_3)_3$

34



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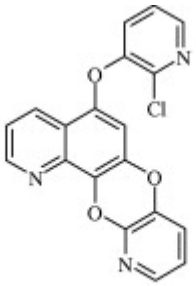

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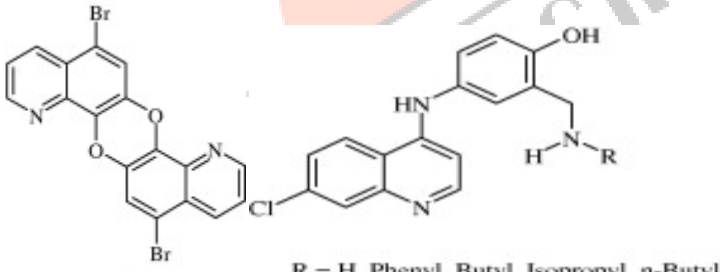


R = H, Phenyl, Butyl, Isopropyl, n-Butyl

37

38

(C)..Antimycobacterial Activity

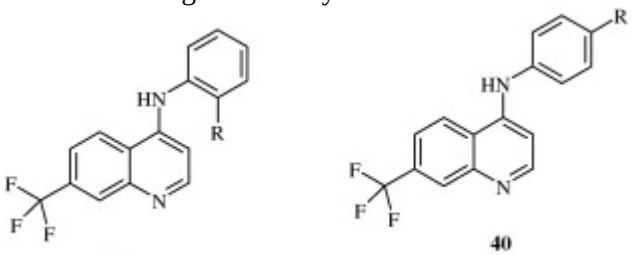
Tuberculosis (TB) has become a global health problem because of lack of proper therapeutic agents for its remedy.There is another serious and alarming problem due to there surgence of TB especially for the synergy with global human immunodeficiency virus (HIV) and the emergence of multi-drug-resistant (MDR) strains. Thus, there is an urgent need for developing new anti-tubercular drugs which will effectively kill MDR strains, less toxic, shortened duration of therapy, rapid mycobactericidal mechanism of action in the intracellular environment. In this direction various quinoline containing molecules have been synthesized tested for anti-TB activity all over the world. D. Sriram *et al.* [25] synthesized 48 novel 6-nitroquinolone-3-carboxylic acids derivatives and compound having R = (4((benzo[*d*][1,3]dioxol-5-yl) methyll)piperazin-1-yl) was found to be the most active compound*in vitro* with MIC of 0.08 and 0.16 µM against MTB and MDR-TB, respectively.

They also extend their work to synthesized various 2-(sub)-3-fluoro/nitro-5, 12-dihydro-5-oxobenzothiazolo[3,2-*a*]quinoline-6-carboxylic acid and evaluated for *in-vitro* against *Mycobacterium tuberculosis* H37Rv (MTB), multi-drug resistant *Mycobacterium tuberculosis* (MDR-TB), and *Mycobacterium smegmatis* (MC2Compound bearing R1=2-(3-

(diethyl carbamoyl) piperidin-1-yl)-) was found to be the most active compound with MIC of 0.18 and 0.08 μM against MTB and MTR-TB [53)

(D). Analgesic activity

4-Substituted-7-trifluoromethylquinolines [**39**, **40**] synthesized by Abadi et al. (2005) have been found to have a good analgesic activity. The activity is attributed to their nitric oxide releasing properties. Gomtsyan et al. (2005) developed a quinoline [**41**] based analgesic agent whose activity was attributed to its antagonism at Vanilloid receptors. A few quinoline derivatives [**42**] developed by Manera et al. (2007) by acting as selective agonists at Cannabinoid CB_2 receptors show their analgesic activity.



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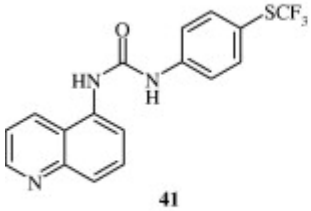

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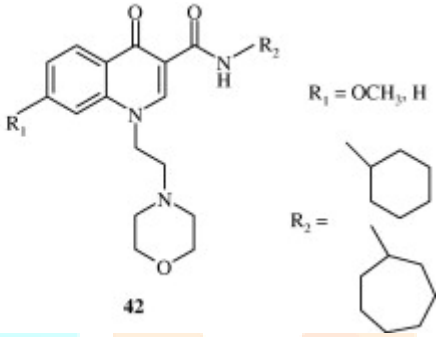

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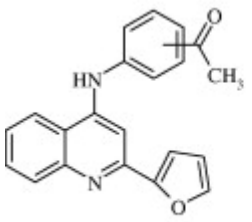
(E).Antimicrobial Activity

The dramatically rising prevalence of multi-drug resistant microbial infections in the past few decades has become a serious health care problem. The search for new antimicrobial agents will consequently always remain as an important and challenging task for medicinal chemists. Quinolones is a special structural class of quinoline antimicrobial agents. It is characterized by 1,4-dihydro-4- oxo-3-pyridine carboxylic acid and a fused benzene ring moiety. Extensive SAR have been established on this nucleus and resulted in number of currently marketed synthetic antimicrobial agent like ciprofloxacin (ofloxacin
and sparfloxacin etc. 1-aryl / heteroaryl-5 methyl-1, 2, 4-triazolo[4,3 a] quinoline derivatives synthesized and tested *in vitro* for their antibacterial activity and compound exhibited MIC 10 mg/ml against salmonella typhae . Shiv P. Singh *et al.* reported 4-(4-pyrozolyl)-2-aminopyrimidines and compound showed moderate activity against
C. albicans, A. niger, Salmonella typhae. V. Jayathirtha Rao *et al.* reported synthesis of some
new multi substituted quinoline by Baylis–Hillman reaction and screened them against no. of Gram-positive organisms, viz., *Bacillus subtilis, Bacillus sphaericus*, and *S. aureus,*and three Gram-negative organisms, viz., *Chromobacterium violaceum, Klebsiella aerogenes*, and *Pseudomonas aeruginosa*
most of compound exerted a wide range of broad spectrum of antibacterial activity. G. Venkat Reddy *et al.* reported a series of novel imidazo fused quinolone carboxamides and evaluated against antibacterialactivity, derivatives exhibit moderate antibacterial activity.(53)

(F). Anti-inflammatory activity

2-(Furan-2-yl)-4-phenoxy-quinoline [**43**, **44**] derivatives developed by Chen et al. (2006) are found to be inhibitors of lysozyme and β-glucuronidase release. Baba et al. (1996) developed a quinoline derivative [**45**] with potent anti-inflammatory effect in adjuvant arthritis rat model. Certain quinoline derivatives [**46**, **47**] have been developed for treating osteoarthritis by Gilbert et al. (2008). These are amino-acetamide inhibitors of Aggrecanase-2.



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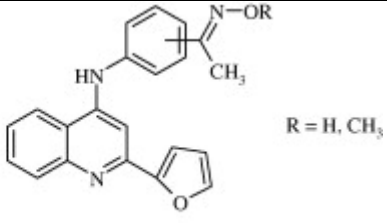
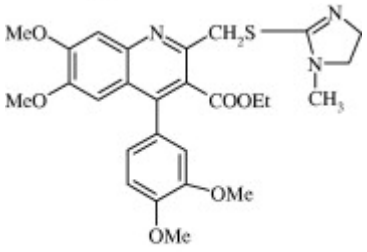


R = H, CH_3

44



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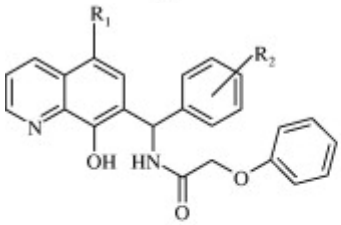
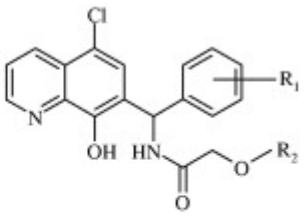


R_1 = H, F, NO_2, Cl

R_2 = H, 4-Cl, 4-CH_3, 4-OCH_3

46

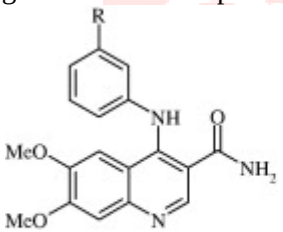


R_1 = H, 4-OCH_3, 3-NO_2

R_2 = Nitrogen Heterocyclic

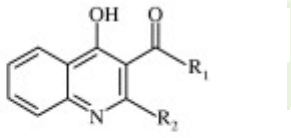
47

(G). Antineoplastic - Some of the amido-anilinoquinolines [**48**] developed by Scott et al. (2009) act as anti-tumour agents by inhibiting CSF-1R kinase. Novel 4-hydroxyquinolines [**49**] synthesized by Mai et al. (2009) are histone acetyl transferase (HAT) inhibitors. Miller et al. (2009) developed a few 3-cyanoquinolines [50] as inhibitors of insulin like growth factor receptors (IGF-1R) for the treatment of cancer.



R = F, Cl, Br, CH_3

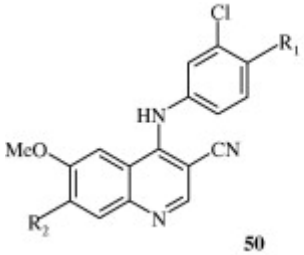
48



R_1 = OH, OEt

R_2 = CH_3, C_5H_{11}, $C_{10}H_{21}$, $C_{15}H_{31}$

49



R_1 = Substituted-2-thioimidazole

R_2 = Substituted nitrogen heterocyclic

50

(H). Cardiovascular Activity

In an attempt to identify potential cardiovascular agent as Ca channel blocker, cAMP phosphodiesterase III etc various chemical modification of quinoline derivatives have attempted with positives results and have come up new lead compounds. John M. MeCall *et al.* reported synthesis and SAR study on a series of 7- (trifluoromethyl)-4-aminoquinoline and evaluated their hypotensive activity. Compound 1-[(4-fluorophenyl) sulphonyl)-4-[4-[(7-(fluoromethyl)- 4-quinolinyl] amino] benzoyl] piperazine. i.e. losulazineselected for clinical development and shows hypotensive. Mannich bases prepared by aminoalkylation of 3Hpyrrolo[3,2-f]quinoline showed vasorelexation in the presence of □-blocker propanolol. B. Bahadir *et al.* effect in rat, cat and dog. Some new 4-(diphenyl methyl)- □-[(4-quinolinyloxy]methyl]-1-piperazinethanol derivatives were also exhibit cardiovascular activity on isolated perfused rat and guinea pig heart and compound DPI 201-106 showed potent inotropic effect in rat heart . Quinoline having pyridazinone moiety were

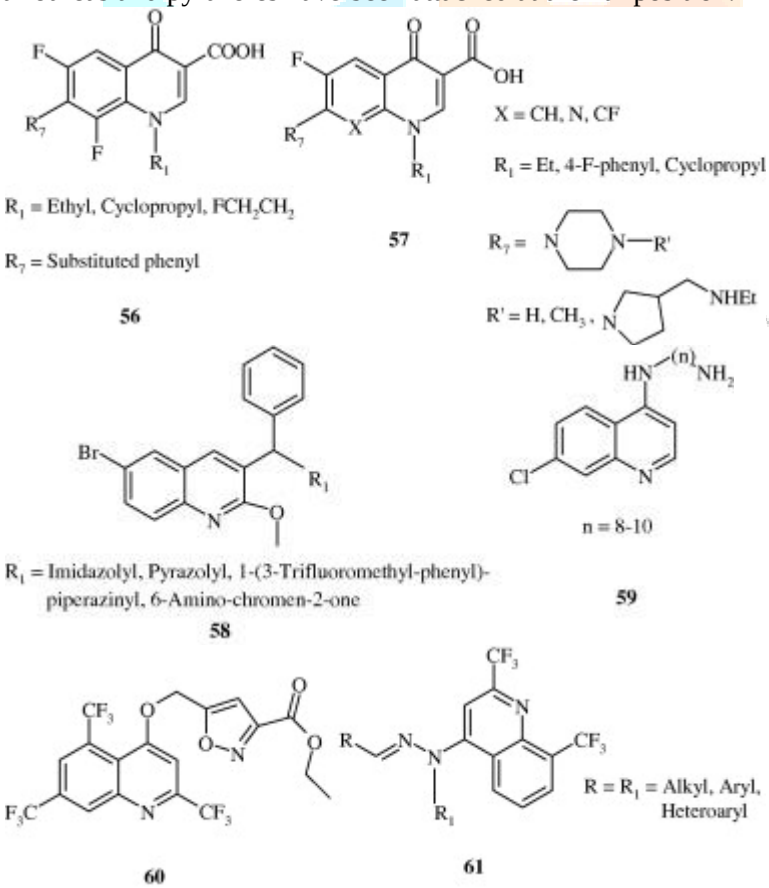
designed and their vasodilator activity was examined on the isolated main pulmonary artery of the rabbit and compounds showed moderate vaso relaxant activity compared with standard drug Milrinone [53]

(I).Anticonvulsant Activity

Epilepsy is a common neurological disorder and a collective term given to a group of syndromes that involve spontaneous, intermittent, abnormal electrical activity in the brain. The maximal electroshock (MES) test and the subcutaneous pentylene tetrazole (scPTZ) test are the most widely used animal models of epilepsy to characterize the anticonvulsant activity of new compounds. In recent years various molecular modifications of quinoline derivatives have been reported with promising anticonvulsant results. Zhe-Shan Quan *et al.* [53] reported a series of 5-alkoxy-[1,2,4]triazolo[4,3-a]quinoline derivative with anticonvulsant activity evaluated by the maximal electroshock test (MES) and their neuro toxicities were measured by the rotarod test. 5-hexyloxy [1,2,4]triazolo[4,3-a] quinoline was found to be most potent anticonvulsant, with median effective dose (ED50) of 19.0 mg/kg.. A fused triazole and triazolone derivatives of quinoline- 2(1*H*)-one and their anticonvulsant activity were reported [39]. Results of the study revealed that triazole, but not the triazolone showed stronger anticonvulsant effects and compound **)**, 5-(*p*-fluorophenyl)-4,5–dihydro-1,2,4- triazolo[4,3-*a*] quinoline, showed the strongest anticonvulsant effect with (ED50) of 27.4mg/kg and 22.0mg/kg in the anti- MES and anti-PTZ test, respectively. Kynurenic acid derivatives analogue 4-urea-5,7-dichlorokynurenic acid were synthesized and subsequently screened in mice for anticonvulsant activity by Nichols, *et al.* most of the compound showed excellent anticonvulsant activity. (53)

(J). Antibacterial

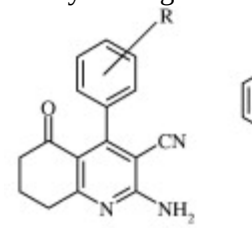
Ma et al. (2009) synthesized phenoxy, phenylthio and benzyloxy substituted quinolones [**56**] with a fair amount of anti-bacterial activity. Sanchez et al. (1988) developed certain 8-substituted quinoline carboxylic acids [**57**] with anti-bacterial activity. Upadhayaya et al. (2009) developed quinoline derivatives [**58**] through molecular modelling techniques which were found to be active against *Mycobacterium tuberculosis* H37Rv strain. These were derivatives of 3-benzyl-6-bromo-2-methoxy quinolines. De Souza et al. (2009) developed 7-chloro quinoline derivatives [**59**] effective against multi-drug resistant tuberculosis. Lilienkampf et al. (2009) developed quinoline based compound bearing an isoxazole containing side chain [**60**] active against *Mycobacterium tuberculosis*. Some novel anti-tubercular quinolines [**61**] have been developed by Eswaran et al. (2010) using mefloquine as the lead, wherein active pharmacophores viz. hydrazones, ureas, thioureas and pyrazoles have been attached at the 4th position.



(K). Antifungal

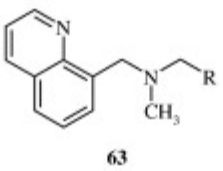
Gholap et al. (2007) developed certain tetrahydroquinolines [**62**] which are found to have a good degree of activity against fungi *Candida albicans*, *Fusarium oxysporum* and *Mucor* sp. Kharkar et al. (2009) developed a series of quinoline derivatives [**63**] using terbenafine as lead as antifungal agents. The developed compounds contained different bulky

aromatic rings in the side chain. The compounds were designed using LeapFrog drug design program. Kumar et al. (2011) developed certain secondary amines [**64**] containing 2-chloroquinoline and evaluated them for their antimycotic activity against *Aspergillus niger*, *A. flavus*, *Monascus purpureus* and *Penicillium citrinum*. These are non-azole antimycotic agents.



R = 4-Cl, 4-F, 3-NO_2, 4-CH_3, 2-Cl, 3,4,5-$(OCH_3)_3$

62



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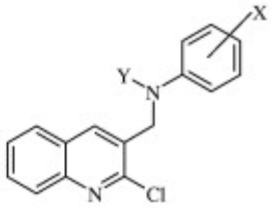


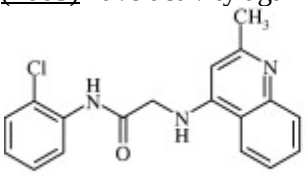
X = F, Cl, Br, CH_3, NO_2, Dichloro

Y = H, CH_3

64

(L). Antiviral

Anilidoquinoline [**65**] derivatives synthesized by Ghosh et al. (2008) are found to have a good degree of *in vitro* activity against Japanese encephalitis virus. Certain quinoline derivatives [**66**] synthesized by Chen et al. (2009) act by behaving as HIV-1 Tat–TAR interaction inhibitors. Massari et al. (2009) developed certain desfluoroquinolines [**67**] for the treatment of HIV infection. Certain mono and polysubstituted quinolines [**68**–**70**] synthesized by Fakhfakh et al. (2003) have activity against HIV-1.



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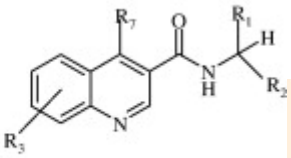

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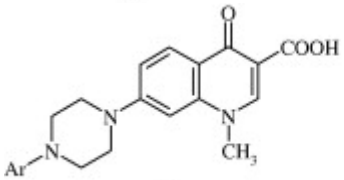

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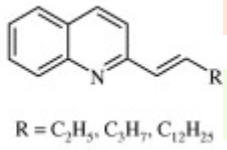
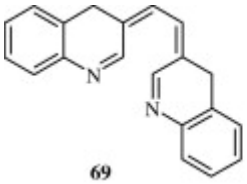


R = C_2H_5, C_3H_7, $C_{12}H_{25}$

68



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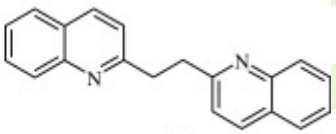
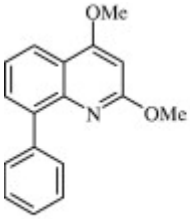


70

3.8. Anthelmintic

Rossiter et al. (2005) synthesized substituted 2,4-arylquinolines [**71**–**74**] which have a good degree of activity against the nematode *Haemonchus contortus*. These arylquinolines maintain their activity against levamisole, ivermectin and thiabendazole resistant strains of *H. contortus*.



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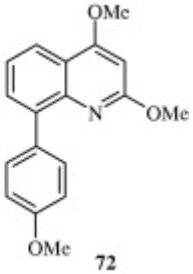

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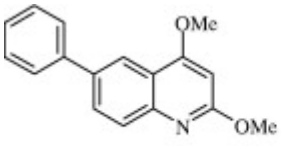

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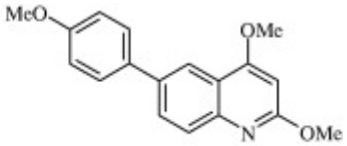

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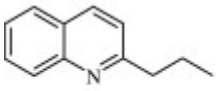
(M). Anti-protozoal

Fournet et al. (1993) found that 2-substituted quinoline alkaloids isolated from *G. longiflora* plant used for the treatment of new world cutaneous leishmaniasis have *in vitro* antileishmanial activity against the extracellular forms of *Leishmania spp*. These include 2-substituted 3-carbon chain quinoline alkaloids and 2-substituted aryl quinoline alkaloids [**75**, **76**]. Alkenyl and alkynyl quinolines [**77**, **78**] developed by Fakhfakh et al. (2003) show activity against the causal agents of cutaneous leishmaniasis, visceral leishmaniasis, African trypanosomiasis and Chagas' disease. Ma et al. (2009) developed certain quinolones [**79**] which had activity against *Trypanosoma cruzi*. Franck et al. (2004) developed quinoline derivatives [**80**, **81**] which showed activity against *T. cruzi*.



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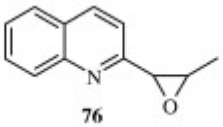

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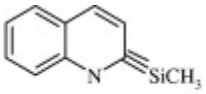

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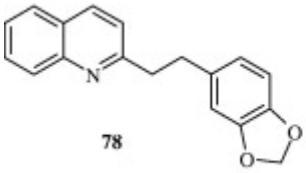

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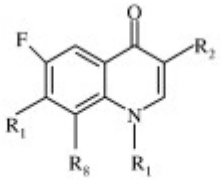
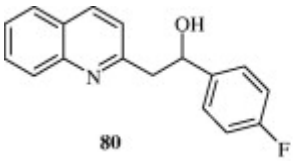


R_1 = Et, Pr, CH=CH_2

R_3 = COOH, COOMe, COOet, $CONH_2$

$R_7 = R_8$ = Substituted Phenyl

79



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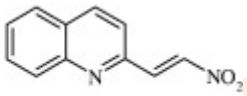
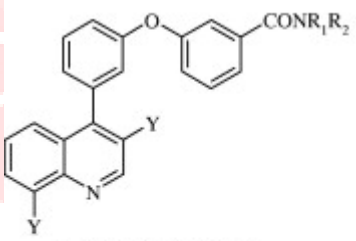


81

(N). Cardiovascular activity

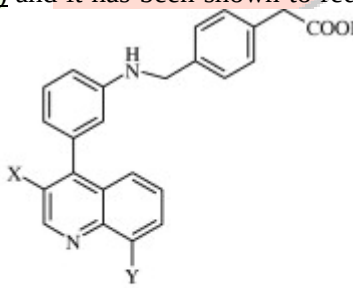
Certain biarylether amide quinolines [**82**] developed by Bernotas et al. (2009) act as liver X receptor agonists and are useful in conditions of dyslipidaemia. These agents also reverse the conditions of arteriosclerosis. A few phenyl acetic acid based quinolines [**83**] developed by Hu et al. (2007) also act as agonists at liver X receptors. These agents have good binding affinity for LXRβ and LXRα receptors. 4-Thiophenyl quinolines [**84**] developed by Cai et al. (2007) are HMG-CoA reductase inhibitors and have utility as hypocholesterolaemic agents. Quinoline-4-carboxylic acids [**85**] synthesized by Lloyd et al. (1994) are angiotensin II receptor antagonists and hence act as hypotensive agents. Hypotensive activity of centhaquin [**86**] has been demonstrated by Srimal et al. (1990) and it has been shown to reduce the blood pressure in cat in a dose dependent manner.



X = CF_3, Cl; Y = CH_2Ph

NR_1R_2 = Methyl ester, Pyrrolidine, Piperidine, Morpholine

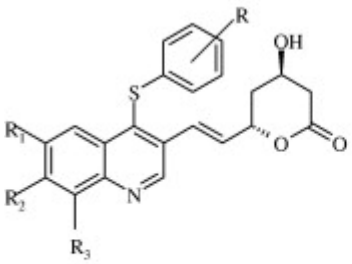
82



X = CH_2Ph, COPh, CN, $CONH_2$

Y = CF_3, CH_3, Cl

83

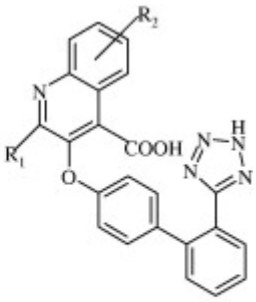


R = 4-$CH(CH_3)_2$, 4-F, 3-OCH_3; R_1 = H, F

R_2 = H, F, Cl or Substituted thiophenyl group;

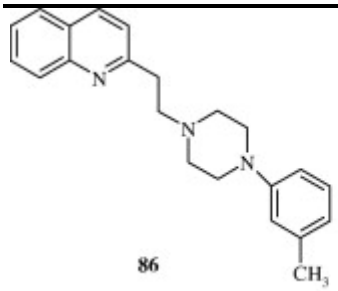
R_3 = H, F or Substituted thiophenyl group

84



R_1 = Pr; R_2 = H

85



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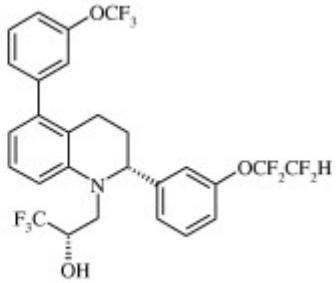

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4. CONCLUSION

These observations shows for the development of new quinoline derivatives that exhibit varied biological activities i.e. anticancer, anti mycobacterial, antimicrobial, anticonvulsant, anti-inflamatoryand cardiovascular activities. the quinoline derivatives are used in as antibacterial drugs and various potent application such as catalyst,dyes-pigment, cosmetics, industrial and pharmacological work. Thus quinoline derivatives is an effective new generation anti infective agent and provide scope to designing molecular imaging experiments which have utility in biological science. A lot of work have been done and more to go. synthesizing of newer quinolines have immense possibilities and scope for drug development. After studying many research paper and jounerals I got a conclusion that quinoline is very sestive to react with other reactants and give many important and effective derivatives .

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