

# A REVIEW ON QUINOLINE AND ITS DERIVATIVES

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**Abstract:** Quinoline is a hygroscopic liquid that is colorless has a pungent odor and Darkens with age. It is soluble in alcohol, ether, benzene, and carbon disulfide and is sparingly soluble in water. Quinoline is a weak tertiary base. It forms salts in acids and exhibits reactions similar to benzene and pyridine, and can engage in both electrophilic and nucleophilic substitution (HSDB), Quinoline, also known as 1-azanaphthalene, 1-benzazine, or benzo[b]pyridine, is a heterocyclic aromatic organic compound. It has the formula C<sub>9</sub>H<sub>7</sub>N. Quinoline structure is known ever since 1908 and proved by total synthesis by Wood ward and Doe ring in 1945. It was the structural model for other anti-malarial quinoline derivatives. It was first isolated by Runge in 1834 from coal tar bases and subsequently, Coal tar remains as the principle source of commercial quinoline; If its aged sample is exposed to light, it turns became yellow and later brown.

**Keywords:** QuinoLine, Pharmaceutical, Heterocyclic.

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## 1. PHARMACOLOGICAL ACTIVITIES OF QUINOLINE AND IT'S DERIVATIVES:

Quinoline is primarily used as the building block to other special chemicals. Approximately 4-tons are produced annuy according to report published in the year 2005. (1) Quinoline is mainly used as the building block to other special chemicals. 8hydroxy quinoline is versatile chelating agent and precursor pesticide. (2) Quinoline is considered likely to be carcinogenic in humans in accordance with proposed EPA carcinogen risk assessment guidelines (U.S. EPA, 1996a) on the basis of observations of exposure-related increased incidence of an unusual malignant tumor in multiple strains of rats and mice, in multiple experiments using oral, dermal, i.p., and s.c. dosing, and at an early age. (3)

Quinoline can be derived from petroleum, coal processing, production and use facilities, and shale oil. It is used as an intermediate in the production of various compounds and paints, and as a solvent for resins and terpenes. Quinoline is also a component of tobacco smoke (HSDB, 1999). Therefore, there is potential exposure of the general population to quinoline in the environment. (4) Malaria is the most lethal human parasitic infection. At present, there are estimated 250 million cases of malaria worldwide. The vast majority of these cases (86%) are in the African region, followed by the South-East Asia (9%) and Eastern Mediterranean regions (3%). There were an estimated 0.881 million deaths worldwide in 2006, of which 90% were in the African region and 4% in each of the South-East Asia and the Eastern Mediterranean regions. (5) Azetidinone derivatives are also reported to have powerful antimicrobial, anti-inflammatory, anticonvulsant, carbonic anhydrase inhibitor, local anaesthetic, anthelmintic, hypoglycemic antitubercular activity, antiviral and hypolipidemic activity. (6-7). Quinoline is one of the most popular N-hetero aromatic compounds incorporated into the structures of many pharmaceuticals. Many quinoline-containing compounds exhibit a wide spectrum of pharmacological activities, such as antiplasmodial, cytotoxic, antibacterial, antiproliferative, antimalarial and anticancer activity, antitumor, immune modulatory, caspase-3 inhibition, antileishmanial, local anesthetic, anti arrhythmic and anti inflammatory activities neuroleptic activity, antihypertensive cytotoxic, antihistamine, CVS, antiseptic, analgesic, antihelmintic, hypnotic

, sedative and CNS(8-30) Based on the structure of the integrase core domain and pharmacophore perception, the quinolone derivative as the lead compound via virtual screen in ACD, MDDR, NCI and Chinese Herb three-dimensional database with the aid of DOCK 4.0 program have been picked out and synthesized by LuoZai-gang et al. (8). Their primary anti-HIV properties against integrase reveal that 6-position methyl group on the benzene ring of quinolone plays a more important role than chlorine, 7-position methyl group or no substituted group. But the title compounds exhibit little difference when the substituted group was phenyl or thienyl on the pyridine ring of quinoline.

Thiadiazole with styryl and quinazoline are reported by Bhandari S et al. (9) to exhibit wide range of anticonvulsant, sedative, tranquilizer, analgesic, antimicrobial, anesthetic, anticancer, antihypertensive, antiinflammatory, diuretic and muscle relaxant properties. With the intention to develop potent anticonvulsant agents it has been designed, synthesized 3-[5-substituted 1, 3, 4-thiadiazol-yl]-2- styryl quinazolin-4(3H)-ones derivatives. The synthesized derivatives have been tested in vivo for their anticonvulsant activity using MES, PTZ and Actophotometer model. Recent developments on antimicrobial quinoline chemistry have been shortly reviewed covered by Carlos M et al (10). On six important topics: Historical aspects of the quinoline-based antimicrobial drug development; Increasing resistance problems and reasons for developing new antimicrobial agents; Molecular quinoline-based hybrids in the design and development of novel antimicrobial agents; Structural evolution of the quinolones as effective agents in the treatment of microbial infections and Design and synthesis of new quinoline-based molecules as potential anti mycobacterial agent Sulfonamide substituted 8-hydroxyquinoline derivatives have been prepared by Ritu B Dixit et al. (11). using a microwave synthesizer. The interaction of sulfonamide substituted 8-hydroxyquinoline derivatives and their transition metal complexes with Plasmid (pUC 19) DNA and Calf Thymus DNA have been investigated by UV spectroscopic studies and gel electrophoresis measurements. The interaction between ligand/metal complex and DNA has been carried out by increasing the concentration of DNA from 0 to 12  $\mu$ l in UV spectroscopic study, while the concentration of DNA in gel electrophoresis remained constant at 10  $\mu$ l. These studies supported the fact that, the complex binds to DNA by intercalation via ligand into the base pairs of DNA.

Kaur K et al. (12). Say that the quinoline scaffold is prevalent in a variety of pharmacology active synthetic and natural compounds. The discovery of chloroquine, the most famous drug containing this scaffold result in control and eradication of malaria for decades. The other known antimalarial drugs from the quinoline family include: quinine, amodiaquine, piperazine, primaquine, and mefloquine. The drugs from this group mostly act during the blood stages of the parasite's life cycle but some like primaquine targets the tissue stages. This review provides a comprehensive literature compilation concerning the study of quinolines and also other heterocycles structure similar to quinoline scaffold in the treatment of malaria. This review covers advances made in the last ten years and it is subdivided into eight subheadings. It consists of discussion on the biological activities, structure activity relationship, and potential biochemical pathway so f4-aminoquinolines, 4-anilinoquinolines, aminoquinolines, quinolines from nature, quinolones, isoquinolines and tetrahydroquinolines, ring-modified quinolines, and miscellaneous quinolines.

Tekwani Babu L et al. (13) Says about recent developments on evaluation of 8-aminoquinoline analogs with broader efficacy and reduced toxicity, which would provide better drugs for treatment of protozoal infections. Recent findings the earlier efforts towards development of 8-aminoquinoline analogs have been directed to extensive derivatization programs. This has led to discovery of tafenoquine for prophylaxis against malaria infections and sitamaquine with utility for treatment of visceral leishmaniasis. Bulaquine, aprimaquine prodrug, has shown reduced methemoglobin toxicity and better malaria-transmission-blocking activity than primaquine. Stereoselective pharmacologic and toxicologic characteristics of chiral 8-aminoquinolines provided the lead for enantiomeric separation of an 8 amino quinoline analog NPC1161B, with greatly reduced toxicity. The antimicrobial activities of 60 natural occurring and synthetic quinolines have been studied by Donnell F et al. (14). The quinolines were organized into seven structural sub groups and, using an in-house microtitre assay, were tested against a range of Gram-positive and Gram-negative bacteria, including a hospital isolate of methicillin-resistant *Staphylococcus aureus* (MRSA). The quinolines exhibiting good bioactivity [i.e. low minimum inhibitory concentration (MIC)] against two *S. aureus* strains have been then assessed for their antimicrobial activity against a range of eight clinically isolated MRSA strains. The study showed that 30 of the tested compounds displayed antimicrobial activity, mostly against Gram-positive bacteria. The effects of substituent groups on the bioactivity of these quinolines have also been discussed. The quinoline 4-hydroxy-3-iodo-quinoline-2-one exhibited significant antimicrobial

activity, being active against the MRSA clinical isolates with MIC values comparable with the antibiotic vancomycin used in the treatment of MRSA infections.

A convenient one-pot preparation of 2-methyl-3-(phenylthiomethyl)quinoline from Morita-Baylis-Hillman adducts via conjugate addition of thiols followed by reductive cyclization with Fe/AcOH was developed Chintakunta R et al.(15). The 2-methyl-3-(phenylthiomethyl) quinolines were transformed into 2-methyl-3-(phenylsulfonylmethyl) quinolines via *m*-CPBA-mediated oxidation.

In the study, a series of thirty-five substituted quinoline-2-carboxamides and thirty-three substituted naphthalene-2-carboxamides have been prepared and characterized by Gonec T et al. (16). They have been tested for their activity related to the inhibition of photosynthetic electron transport (PET) in spinach (*Spinacia oleracea* L.) chloroplasts. Primary *in vitro* screening of the synthesized compounds have been also performed against four mycobacterial species. *N*-Cycloheptylquinoline-2-carboxamide, *N*-cyclohexylquinoline-2-carboxamide and *N*-(2-phenylethyl)quinoline-2-carboxamide showed higher activity against *M. tuberculosis* than the standards isoniazid or pyrazinamide and 2-(pyrrolidin-1-ylcarbonyl)quinoline and 1-(2-naphthoyl)pyrrolidine expressed higher activity against *M. kansasii* and *M. avium* Paratuberculosis than the standards isoniazid or pyrazinamide.

In the study, a series of twelve ring-substituted 4-hydroxy-1*H*-quinolin-2-one derivatives have been prepared by Jampilek J et al. (17). The compounds have been analyzed using RP-HPLC to determine lipophilicity and tested for their photosynthesis-inhibiting activity using spinach (*Spinacia oleracea* L.) chloroplasts. The synthesized compounds have been also evaluated for antifungal activity using *in vitro* screening with eight fungal strains. For the compounds, the relationships between the lipophilicity and the chemical structure of the studied compounds are discussed, as well as their structure-activity relationships (SAR). Sixteen C-2-substituted quinolines have been tested in both human cancer cell lines (MCF-7, H-460 and SF-268) and normal cell lines (Vero and THP-1) by Kouznetsov Vladimir V et al. (18). Biological activity and SAR results have been compared with different molecular descriptors determined *in silico* using online available software, in an attempt to show a relationship with the possible mode of action of these quinoline derivatives.

Quinoline-2-carbohydrazide obtained from quinaldic acid has converted to the corresponding carbothioamide by treatment with benzyliso (thio) cyanate. The newly synthesized compounds have been characterized by elemental analysis by Muhammet O et al. (19). The antimicrobial activity study revealed that some of the newly synthesized compounds showed good to moderate activity against a variety of microorganisms.

Yellappa S et al. (20) have synthesized a series of novel quinoline-6-carboxamides and 2-chloroquinoline-4-carboxamides. By the reaction of their analogous carboxylic acids with various amine derivatives in the presence of base TEA and protecting agent BOP at room temperature. Synthesized compounds have been confirmed by spectral characterization viz IR, <sup>1</sup>H-NMR, and MS. Antibacterial activity carried out against *Escherichia coli* and *Staphylococcus aureus* indicated that the synthesized compounds have been active against these microorganisms.

Horowitz E et al. (21) describes the synthesis of a new bis-bifunctional derivative of 8-hydroxyquinoline, its reaction with a number of divalent, first-row transition metals to form coordination polymers, and a thermogravimetric study of the thermal stability of the polymers. The ligand, 5,5'-[methylenebis(p-phenylene)trilomethyldiene] di-8-quinolinol was prepared in a condensation reaction between 5-formyl-8-hydroxyquinoline and 4,4'-methylenedianiline and subsequently treated with the acetate salts of Mn(II), Co(II), Ni(II), Eu(II), and Zn(II). The metal coordinated in the backbone of the polymer is shown to be an important factor in governing the thermal stability when the samples are heated in vacuum.

Novel derivatives of 6*H*-indolo [2, 3-*b*] quinoline substituted at C-2, C-9 or N-6 positions with *O*-*L*-daunosamine or *L*-acosamine connected with the chromophore *via* an alkoxy or alkyl linker have been synthesized by Badowska R K et al. (22). The obtained compounds have been evaluated *in vitro* for their cytotoxic activity against several cell lines of different origin and tested for their ability to influence the cell cycle using the flow cytometric analysis. The compounds tested show cytotoxic activity against A549, MCF-7 and Hs294T cells and overcome multidrug resistance in colorectal adenocarcinoma LoVo/DX, uterine sarcoma MES-SA/DX5 as well as promyelocytic leukemia HL-60/MX2.

A series of lanthanide nitrate complexes with *N*-(furfuralidene)-*N*-( $\epsilon$ -isonicotinoyl)hydrazine (INHFF) have been synthesized by Satyabhama D S et al.(23). These complexes have been characterized by elemental analysis, conductance, magnetic moment measurements, and I.R, UV-visible, TGA-DTA and luminescence studies. In these complexes the

hydrazone, N-(furfuralidene)-N $\epsilon$ -isonicotinoylhydrazine behave as a neutral bidentate ligand with the carbonyl oxygen and azomethine nitrogen as two coordinating sites. The three nitrate ions also coordinate unidentately with seven coordinate for the lanthanide (III) ions with tentative monocapped octahedral geometry for the complexes. the complexes have a general formula, [Ln (L) 2(NO<sub>3</sub>)<sub>3</sub>] where Ln= Pr (III), Nd (III), Sm (III), Gd (III) or Tb (III) and L= N-(furfuralidene)-N $\epsilon$ -isonicotinoylhydrazine. Spectroscopic determination of nephelauxetic ratio ( $\beta$ ), covalency factor (b1/2), Sinha parameter ( $\delta$  %) and covalency angular overlap parameter ( $\eta$ ) show a weak covalent bond formation between the metal ion and the ligand in the complexes.

Quinoline derivatives have been synthesized by Ramin Z et al.(24).and explored for their anticancer, antitnephritic, antitumor, anti-inflammatory and analgesic activity, as antiergetic agents for treating Alzheimer's disease (AD). Possible formation of 5- and 7-substituted quinolines during the Skraup reaction using m-substituted anilines is well understood. However, there are conflicting reports on the composition of the products from certain reactions

Novel quinoline derivatives have been designed by Maciejat S.et al. (25). as anticancer iron chelators. Structure they combine active moieties of known quinoline and thiosemicarbazone bioeffectors. For the synthetic part of study, applied microvawe assisted techniques MAOS. Resulted compounds exhibited interesting anticancer activities against HCT116 cancer cells.

By Saeed B et al (26) a simple and fast three-component synthesis of new and biologicly active hexahydro-2-quinolinecarboxylic acid scaf-fold 4 has been carried out using cyclocondensation reaction of arylmethylidenepyruvic acids 1,1,3-cyclohexandiones and ammonium acetate under solvent-free conditions and at room temperature. This protocol has the advantages of facility, easy work-up, high yields, short reaction time and environmenty friendly character

Quinoline derivative have been synthesized by Pawar P Y et al.(27) by the reaction of resorcinol with ethyl acetoacetate yielded the 7-hydroxy-4-methyl coumarin, which on treatment with substituted thiadiazole in presence of glacial acetic acid gives 7-hydroxy-4-methyl-1-5-phenyl-1,3,4-thiadiazole-2yl,quinoline-2(1H)-one. Purity of synthesized compound has checked by TLC and IR, 1H NMR and elemental analysis, has elucidated structures. The synthesized compounds have been screened for anticonvulsant activity.

The required quinoline based compounds have been prepared by Vora P J et al.(28) by reaction of aryl amine and ethyl acetoacetate via 4-aminobenzaldehyde (6-ethoxy-2-methylequinolin-4-yl) hydrazone and substituted diazotizedsulfonamides to 4-[(4-aminophenyl) (6-ethoxy-2-methylequinolin-4-yl) carbonohydrizonoyl diazenyl] substituted benzenesulfonamides. The resulting newly synthesized compounds are characterized by elemental analysis, IR, 1H NMR and 13C NMR. the newly synthesized compounds have been evaluated for their antibacterial activity towards two Gram positive and two Gram negative bacteria and antifungal activity towards Aspergillus Niger and Candida albicans. Some selected synthesizes compounds have also been evaluated for their antitubercular activity with mycobacterium tuberculosis bacilli. The results obtained from antimicrobial activity are found that some compounds have higher antibacterial activity and antifungal activity, where as the rest of the compounds show varying activity. Some of the selected compounds show higher antitubercular activity.

Acording to Desoky E et al. (29) Quinoline-2-carbohydrazide react with aryl or alkyl isothiocyanates to give the corresponding quinoline thiosemicarbazides. Cyclization of the substituted thiosemicarbazides with sodium hydroxide led to the formation of 5-(quinolin-2-yl) - 2H-1, 2, 4-triazole-3(4H)-thiones (5a-e). Desulfurization of thiosemicarbazides by mercuric oxide gave 5-(quinolin-2-yl)-1, 3, 4-oxadiazol- 2-amines (6a-e). Treatment of thiosemicarbazides with ethyl bromoacetate or -bromopropionic acid yielded (Z)-N'-(3-substituted thiazolidin-4-oxo-2-ylidene) quinoline-2-carbohydrazides, respectively. Treatment of thiosemicarbazides with chloroacetone furnished (Z)-N'-(4-methyl-3-substituted-thiazol-2(3H)-ylidene) quinoline-2-carbohydrazides. Furthermore, the reaction of thiosemicarbazides with phosphorus oxychloride gave N-substituted-5-(quinolin-2-yl)-1,3, 4-thiadiazol-2-amines. newly synthesized compounds have been tested and evaluated for antimicrobial activity.

The series of eight substituted amides of 5-hydroxy-2-methylquinoline-7-carboxylic acid have been prepared by Musiol R et al.(30). The synthetic procedures of the compounds are presented. the prepared quinoline derivatives have been analyzed using RP-HPLC method for the lipophilicity measurement and their lipophilicity was determined. The prepared compounds were tested for their photosynthesis-inhibiting activity (the inhibition of photosynthetic electron

Novel ligand containing 8-hydroxyquinoline (HQ) moiety has been prepared and characterized by Vashi R T et al. (31). For synthesis of ligands a hydroxyquinoline-5-carbaldehyde has been treated with phenyl hydrazine to synthesis corresponding hydrazone. The hydrazone has been condensed with diazonium salt of sulfanilamide to synthesis formazan. The formazan has been converted to corresponding tetrazolium salts by using hydrogen peroxide, hydrobromic acid and ferrous sulphate. The novel ligand undergo the chelating reaction with Cu (II), Ni (II), Co (II), Mn (II), Zn (II) and Fe (III) salts to prepare transition metal chelates. These chelates have been characterized by physicochemical methods such as elemental analysis, magnetic susceptibility, IR and electronic spectral data. The stoichiometry of the complex has been found to be 1: 2 (Metal: ligand) for divalent and 1:3 for trivalent ions. An octahedral geometry around Co (II), Ni (II), Fe (III) and Mn (II), distorted octahedral geometry around Cu (II) and tetrahedral geometry around Zn (II) have been proposed. The antimicrobial activity of ligand and its metal chelates had been conducted against various bacteria.

Polymer has been synthesized by Mandavgade Shailesh K et al. (32) from the polymerization of 8-hydroxyquinoline 5-sulphonic acid and catechol with formaldehyde (8-HQ- 5- SACF) by solution condensation in an acid medium. The polymer has been characterized by elemental analysis, UV-Visible spectra, FTIR and NMR spectroscopy. The thermal stability of the polymer has been determined by TGA. In addition, the activation energy for the formation of polymer has been calculated using TGA data by Freeman-Carroll method and Sharp-Wentworth method. The surface features of the polymer have been analyzed by scanning electron microscopy (SEM). The thermodynamic parameter such as free energy change ( $\Delta F$ ), entropy change ( $\Delta S$ ), Apparent entropy change ( $S^*$ ) and frequency factor Z are also determined on the basis of TGA curve and by using data of Freeman-Carroll method. A new series of quinoline derivatives 2-chloro 3-formyl quinoline, 3-chloro-4(2-chloroquinolin-3-yl) 1-phenyl amine azetidin 2-one, 3-chloro-4(2-chloroquinolin-3-yl)2,4- dinitro phenyl amine azetidin 2-one, 3-chloro-4(2-chloroquinolin-3-yl) 4-nitro phenyl amine azetidin 2-one, 3-amino 1H-pyrazoloquinoline, 3-diazo-1H-pyrazoloquinoline, 6-methoxy-1- phenyl pyrazolo quinoline have been synthesized by 4 scheme methods, containing various steps by Muthumani P et al (33). The structures of the synthesized compounds have been established on the basis of physical and spectral data and are screened for diuretic and antimicrobial activities, some of the exhibited significant activity.

Quinoline is a heterocyclic scaffold of paramount importance to human race. The utility of quinoline derivatives in the areas of medicine, food, catalyst, dye, materials, refineries and electronics is well established. As a result, the synthesis of quinoline core and its derivatives have been an attractive goal for the synthetic organic chemist. In the recent past there have been several new developments in the chemistry associated with quinolines. In pursuit to develop easy and practical approaches to a variety of quinoline derivatives decorated with useful pharmacophores different research workers have made use of new catalysts, medium or physical conditions in several well established synthetic methodologies. Besides an array of new and innovative strategies from novel substrates have been developed by Madapa et al. (34) which has rendered the synthesis of quinoline core a much simpler process as compared earlier. An assimilation of the literature related to the advances in the syntheses of quinolines and quinoline-annulated ring systems since 2005 is being presented here.

Some new 7-chloro-4-aminoquinoline derivatives have been prepared by Rudrapal M et al. (35) by modification at C-2 position of six membered 1, 3-thiazinan-4-one ring system attached at the terminal propyl side chain of 7-chloro-4-aminoquinoline nucleus. The synthesized compounds have been characterized by their physical, analytical (CHN) and spectral data (UV-Visible, IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR and MS). In addition to evaluation of antimalarial activity, the synthesized compounds have been evaluated for antibacterial activity against six different strains of Gram positive (*Bacillus subtilis*, *Bacillus cereus*, *Staphylococcus aureus*) and Gram negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*) at two different tested doses viz. 25 mg/disc and 50 mg/disc by disc diffusion method. The compounds have been found to be active against the tested organisms, but have been active as compared to standard drug ofloxacin (5 mg/disc). The compounds with aromatic bulky substituents such as 2-fluorophenyl-, 3-hydroxyphenyl-, 4-methoxyphenyl-, furan-2-yl, 4-(dimethylamino)phenyl-, 5-methylthiophen-2-yl at C-2 position of 1,3-thiazinan ring system showed better antibacterial activity than that of the compounds with aliphatic alkyl (ethyl) substituent. It indicates that aromatic bulky.

By Oprea Gabriela Maria et al (36). The influence of temperature and collector concentration on its adsorption rate on mineral surface was studied as regarding the 8-hydroxyquinoline/smithsonite system. Theoretical equations as well as experimental data may be useful to estimate the adsorption rate and kinetics connected to the conditioning stage in

mineral flotation in order to optimize the selectivity and the recovery of the valuable mineral substituents have greater contributing effect to the antibacterial activity of the 7-chloro-4-aminoquinoline derivatives as compared to aliphatic non-bulky group. The interaction between donor 8-hydroxyquinoline (HQ) and  $\pi$  - acceptor 1, 4-benzoquinone (BQ) has been studied by Ibrahim Asmaa A et al.(37) in the solution as well as in the solid state. Infrared spectroscopic data indicate that a charge transfer interaction between the donor and acceptor are due to  $\pi \rightarrow \pi^*/ n \rightarrow \pi^*$  transition by the formation of radical ion pairs. In solution state, the formation constant, the extinction coefficient, the free energy and transition energy of the resulting charge transfer complex (CTC) were determined. The optimum experimental conditions, such as time, temperature and solvents for the CTC formation have been established. At various times hydroxyquinolines have been tested for antibacterial activity (von Oettingen. 1933), but never under conditions where their relative potencies could be assessed. The best known of the seven isomerides is 8-hydroxyquinoline, also known as oxine. The familiar Chinosol of commerce is a mixture of oxine sulphate and potassium sulphate. Albert A et al. (38)

A series of potentially active quinoline based azetidinones and thiazolidinones analogues have been synthesized by Mistry B et al.(39) by simple and efficient synthetic protocol. The tetrazole nucleus formed from 2-chloroquinoline-3-carbaldehyde using p-toluenesulphonic acid and sodium azide followed by reaction with various substituted amine to form the corresponding schiff base intermediates. Attempt made to derive final azetidinone and thiazolidinone analogues from Schiff base intermediates by using chloroacetyl chloride and 2-mercapto acetic acid respectively. The newly synthesized analogues have been then examined for antimicrobial activity against some human pathogenic bacterial and fungal strains as 2 gram -Ve bacteria (*E. coli*, *P. aeruginosa*), 2 gram +Ve bacteria (*S. aureus*, *B. subtilis*) and 2 fungal species (*C. albicans*, *A. niger*) to develop novel class of anti microbial agents with varied mode of action.

Quinoline is mainly used as the building block to other special chemicals. Its principle use is a precursor for 8-hydroxyquinoline which is versatile chelating agent and precursor to pesticide. A series of N-(quinoline-4-yl-methylene) benzene imine derivatives has been synthesized by Kannappan N et al.(40) by reaction between quinoline-4-carboxaldehyde and some aromatic and heterocyclic aniline to yield the Schiff's bases. The structure of newly synthesized

Compounds have been confirmed by the analytical and spectral data's (FTIR, <sup>1</sup>HNMR, MS). Data show the positive results, and indicates that the formation of the product takes place and the compounds show the satisfactory yields.

The Density Functional Theory (DFT) and *ab initio* (HF and MP2) calculations were performed by Ebenso Eno E et al. (41) on the quinoline molecule (QL) and its derivatives, namely quinaldine (QLD) and quinaldic acid (QLDA) to investigate their possible role as corrosion inhibitors for mild steel in acidic medium. Calculations have been done for non-protonated and protonated forms *in vacuo* and in water. Some quantum chemical parameters were calculated and discussed in order to provide insight into the reactivity and selectivity of the molecules. The performance of the different calculation methods have been also compared with available experimental data. A comparison in the trends of the quantum chemical parameters in water solution and *in vacuo* shows minimal influence of the solvent effects.

Quinoline (QL) and its derivatives namely quinaldine (QLD) and quinaldic acid (QLDA) have been tested by Ebenso Eno E et al. (42) as inhibitors for the corrosion of steel in 0.5 M HCl by weight loss method at 30 and 40°C. Inhibition efficiency increased with increase in the concentration of the studied compounds but decreased with increase in temperature. Results show that the order of inhibition efficiency is QLDA > QLD > QL. The adsorption of the inhibitors on the steel surface obey Langmuir and kinetic thermodynamic models.

Quinolines are an important group of organic compounds where several compounds containing a quinoline residue are known to possess useful biological activity and used as antibacterial, antifungal and antitumor agents. These pharmacological properties of quinolines aroused our interest in synthesizing several new compounds featuring heterocyclic rings of the quinoline derivatives linked to amino acid ester sidechains with the aim of obtaining a pharmacology active compounds. Methods: Quinoline was N-alkylated by the bromoacetic acid and then oxidized with an alkaline potassium ferricyanide solution to get N-alkylatedquinolone. Conventional solution method for peptide synthesis used as a coupling method between the carboxy-protected amino acids with the acetic acid side chain of quinolone. The DCC/ HOBt coupling reagents used for the peptide bond formation. The proposed analogues were successfully synthesized by Sagheer Othman M et al. (43) and their structural formulas have been consistent with the proposed structures as they were characterized and proved by thin layer chromatography (TLC), melting point, infrared spectroscopy (IR) and elemental microanalysis. tested analogues showed cytotoxic activity on the HEp-2 cell line (tumor of larynx) with inhibitory concentration percent of (IC %) range (49.01 - 77.67%)

The Quinoline and Isoquinoline nucleus is found to be very important in pharmacy field. In recent years, a lot of synthetic drugs have been synthesized in different yield. Pandeya S N et al. (44) reviewed that several other synthetic approaches are discussed involving easily available chemicals and producing high yields.

Mixed ligand complexes of dioxouranium (VI) of the type  $[UO_2(Q)(L) \cdot 2H_2O]$  have been synthesized by Patil Sunil S et al. (45) using 8-hydroxyquinoline(HQ) as a primary ligand and amino acids (HL) such as L-threonine, L-tryptophan, and L-isoleucine as secondary ligands. The metal complexes have been characterized by elemental analysis, electrical conductance, magnetic susceptibility measurements, and spectral and thermal studies. The electrical conductance studies of the complexes indicate their nonelectrolytic nature. Magnetic susceptibility measurements revealed diamagnetic nature of the complexes. Electronic absorption spectra of the complexes show intraligand and charge transfer transitions, respectively. Bonding of the metal ion through N- and O-donor atoms of the ligands is revealed by IR studies, and the chemical environment of the protons is confirmed by NMR studies. The thermal analysis data of the complexes indicate the presence of coordinated water molecules. The agar cup and tube dilution methods have been used to study the antibacterial activity of the complexes against the pathogenic bacteria *S. aureus*, *C. diphtheriae*, *S. typhi*, and *E. coli*.

Sulfonamide substituted 8-hydroxyquinoline derivatives have been prepared by Dixit Ritu B et al. (46) using microwave synthesizer. The interaction of sulfonamide substituted 8 hydroxy quinolone derivatives and their transition metal complexes with Plasmid (PUC 19) DNA and Calf Thymus DNA have been investigated by UV spectroscopic studies and gel electrophoresis measurements. The interaction between ligand/metal complexes and DNA was carried out by increasing the concentration of DNA from 0 to 12  $\mu$ l in UV spectroscopic study, while the concentration of DNA in gel electrophoresis remained constant at 10  $\mu$ l. These studies supported the fact that, the complex binds to DNA by intercalation via ligand into the base pairs of DNA. The relative binding efficacy of the complexes to DNA was much higher than the binding efficacy of ligands, especiy the complex of Cu-AHQMBSH had the highest binding ability to DNA. The mobility of the bands decreased as the concentration of the complex was increased, indicating that there was increase in the interaction between the metal ion and DNA. Complexes of AHQMBSH were excellent for DNA binding as compared toHQMABS.

5-Acyl-8-hydroxyquinoline-2-(3'-substituted-4'-aryl-2, 3—dihydrothiazol 2'ylidene) hydrazones, were prepared by Hussein Mostafa A et al. (47) by the reaction of appropriate 5-acyl-8-hydroxyquinoline-4-substituted thiosemicarbazones and phenacyl bromides. Structures of the new compounds have been verified on the basis of spectral and elemental analyses. Twenty-eight new compounds have been tested for their possible antimicrobial activities. Most of the tested compounds showed weak to moderate antibacterial activity against most of the bacterial strains used in comparison with gatifloxacin as a reference drug. The test compounds showed weak to moderate antifungal activity against tested fungi in comparison with ketoconazole as a reference drug. On the other hand, the newly synthesized compounds were tested for their anti-inflammatory effects and most of them showed good to excellent anti-inflammatory activity compared to indomethacin. Moreover, ulcerogenicity and the median lethal dose of the most active anti-inflammatory compounds were determined in mice; they were non-toxic at doses up to 400 mg /kg after *i.p.* administration.

Thakur Alok Singh et al. (48) find that reaction of aryl compounds containing primary amine with acetic anhydride gave the compound. Which on further treatment with Vilsmeier –Haack reagent (DMF+ POC13) gave the fused pyridine ring by cyclization, which gave compound 2-chloroquinoline-3-carbaldehyde and 2-chloro-9H-pyrido [2, 3-b] indole-3-carbaldehyde respectively. These compounds have been containing the free aldehyde group in their structure which form schiff base on treatment with the different substituted aniline this has because off the presence of primary amine group. These compounds were containing quinoline and pyrido indole with schiff base (substituted –N-((2-chloroquinolin-3-yl) methylene) benzenamine and substituted –N-((2-chloro-9H-pyrido [2, 3-b] indol-3-yl) methylene) benzenamine which showed antimicrobial activity due to the presence of these potent groups in their structure.

Some of alkyl- and alkylamino- derivatives of 6H-indolo [2, 3-b] quinolines are known to be active antiproliferative and cell cycle modulating compounds. Their cytotoxic properties are, at least in part, due to DNA intercalation ability and topoisomerase II inhibition activity. To improve physicochemical and biological properties of 6H-indolo[2,3-b]quinolines the series of new, saccharide (C-2, C-9 or N-6) derivatives have been designed and synthesized by Godlewska Joanna et al (49). The influence of different carbohydrate units (D-glucose, D-lactose, L-rhamnose, Lacosamine, L-daunosamine), position of attachment and linker size on cytotoxic properties and topoisomerase II inhibition activity were tested. Among compounds tested there have been 2-deoxy- $\alpha$ -D-glucopyranosid, 2-deoxy- $\alpha$ -L-rhamnopyranoside and 2-deoxy-  $\alpha$  -D-

lactopyranoside derivatives in the group of saccharide moiety containing compounds and a-L-daunosaminide and a-L-acosaminide in the amino saccharide derivatives series.

A series of new quinoline derivatives incorporating chalcone, pyrazole and pyridine moieties using 5, 7-diiodo-8-hydroxy quinolines starting material have been synthesized and tested by Fahmy Hoda H et al. (50) for their in vitro antimicrobial activities against Gram-positive *Bacillus subtilis*, Gram-negative *Escherichia coli* and fungi *Candida albicans* and *Aspergillus niger*. Some of the tested compounds showed significant antimicrobial activity and the results suggest that [Ethyl 3-(5, 7-diiodoquinolin-8-yl)oxy] propanoate would be potent antifungal activity against *A. niger*, having inhibition zones two times more than the standard drug (Nystatin) and might thus provide a new class of lead structures in the search for novel antifungal agents.

Treatment of 8-hydroxyquinoline and 8-hydroxy-2-methylquinoline with  $\alpha$ -cyano-*p*-chloro/ bromo cinnamionitriles provided 4*H*-pyrano[3,2-*h*]quinoline-3-carbonitrile derivatives, while treatment of (*E*) 2-(4-chlorostyryl)-8-hydroxyquinoline 7 with  $\alpha$ -cyano-*p*-chloro/bromocinnamionitriles and ethyl  $\alpha$ -cyano-*p*-chloro/bromocinnamates provided 4*H*-pyrano[3,2-*h*]quinoline-3-carbonitrile derivatives and ethyl 4*H*-pyrano[3,2-*h*]quinoline-3-carboxylate derivatives respectively. Interaction of 8-hydroxyquinoline and 8-hydroxy-2-methylquinoline with  $\alpha$ -cyano-*p*-fluorocinnamionitrile afforded 2-[4-(piperidin-1-yl) benzylidene] malononitrile via a nucleophilic aromatic substitution reaction. The reactivity of 2-hydroxyquinoline and its 2-substituted derivatives towards  $\alpha$ -cyano-*p*-chloro/bromo-cinnamionitriles and ethyl  $\alpha$ -cyano-*p*-chloro/bromocinnamates are discussed by Agrody Ahmed M et al. (51) in this work. Structures of these compounds were established on the basis of IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR, <sup>13</sup>C NMR-DEPT and MS data.

Recently, the Pyrazolo quinoline (PAQ) derivatives have been used by Pan Jiunn-Hung et al. (52) as a dopant in the multi-layer OLED fabrication. The semiempirical AM1, ZINDO and ab initio DFT B3LYP calculation methods were used to calculate the maximum excitation wavelength ( $\lambda_{max}$ ) and fluorescence wavelengths ( $\lambda_{emi}$ ) of a series of PAQ derivatives based on their optimized structures. The substitution effects of PAQ derivatives with electron-withdrawing and electron-donating substituents have been investigated according to their photo-physical properties and electroluminescence behavior. The calculated TD/DFT/B3LYP/6-31G\* has the better linear relationship of them. Presumably, the procedures of theoretical calculation would be employed to predict the electroluminescence characteristics of the other material, and could give a possible way to design novel material for OLED.

Novel symmetric double quinoline derivatives have been synthesized by Aghera V K et al. (53) using the Vilsmeier-Haack reagent and symmetric double acetamides of 1, 1'-bis(*R*,4-aminophenyl)cyclohexane/methane. The structure of the intermediates (SDA-1 to SDA-3) and final products (SDQ-1 to SDQ-3) were supported by UV, FTIR, <sup>1</sup>H NMR, <sup>13</sup>C NMR and Mass spectroscopic measurements. Compounds SDA-1 to SDA-3 and SDQ-1 to SDQ-3 possess moderate to good antibacterial and antifungal activities.

The photosensitized reaction of 8-hydroxyquinoline 5-sulphonic acid has been studied by Nakinbhaijani Krupa, et al. (54) in the alkaline medium in the visible light using Methylene blue (MB) as photosensitizer. The rate of the reaction has been calculated. The effect of the parameters like pH, concentration of the sensitizer, concentration of the substrate, and intensity of the light on the rate of the photosensitized reaction has been studied. The reaction has been studied in anaerobic condition to observe the effect of the oxygen. Methanol shows free radical scavenging effect. The quantum efficiency of the photosensitized reaction has been calculated. Antimicrobial agents are widely used in the management of infectious disease but most of them have developed resistance to micro-organisms. The cinchophen, which is a water insoluble compound, has reported antimicrobial activity. To overcome this problem and to lower the side effects, many approaches can be utilized and Mannich base approach is one of them. Jumade P P et al. (55)

Studied cinchophen having carboxylic acid (-COOH) group has been converted to amide (-CONH<sub>2</sub>) and it is utilized to synthesize Mannich bases. At first cinchophen, was synthesized by Doebner synthesis, and then it was converted to cinchophen chloride, using oxalyl chloride. Cinchophen chloride was converted to cinchophen amide using ammonia. The Mannich bases have been synthesized by reaction of cinchophen amide with formaldehyde and secondary amine. The prepared Mannich bases have been subjected to physicochemical studies like melting point determination, TLC and % yield. The structures of Mannich bases have been characterized by UV, IR, Mass and NMR spectroscopy. Antibacterial screening of newly synthesized compounds was carried out against *E. coli*, *P. aureoginosa*, *S. aureus* and antifungal activity against *C. albicans* and *A. Niger* according to cup-plate method. The synthesis and in vitro antimicrobial evaluation of several quinoline derivatives of glyoximes have been described by Sevgi Fatih and Bedük A Dincer et al. (56).



Treatment of some aminoquinolines with *anti*-chloroglyoxime gave three new compounds as a ligand. The new ligands have been characterized by elemental analyses, FT-IR and <sup>1</sup>H-NMR. Their antibacterial activities against five Gram-negative (*Escherichia coli*, *Salmonella enteridis*, *Enterococcus faecalis*, *Klebsiella pneumonia* and *Pseudomonas aeruginosa*) and four Gram-positive (*Streptococcus mutans*, *Bacillus cereus*, *Staphylococcus aureus* and Methicillin-resistant *S. aureus*) and antifungal activities against *Candida albicans* have been measured by using disc diffusion and broth microdilution techniques. The minimum inhibitory concentration (MIC) values were calculated by microplate reader at 620 nm. It was found that *N*-(8-hydroxyquinolin-5-yl)-aminoglyoxime moderate antibacterial and antifungal activity against testmicroorganism including MRSA (Methicillin-resistant *Staphylococcus aureus*). New developments in the chemistry of quinoline derivatives were reviewed by Kouznetsov Vladimir V et al. (57).

Studies on the derivative micellar spectral analysis and biological evolution of Pr (III)-8HQ complexes and Effect of solvent on sensitivity of hypersensitive transition for Pr (III) complexes with Quinolone derivatives in doped system and Calculation of Electrostatic, Spin-Orbit Coupling and Configuration-Interaction Parameters For Ln(III) Bioactive System in UV-Visible Region was carried out by *Jatolia et* (58-60).

## 2. CONCLUSION

Quinolone and its derivatives is an important compound which are pharmaceutical ingredients in several drugs due to their potential anti-inflammatory, antitumor, antihyperlipidemic, and antihypertensive properties, among several other biological properties.

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