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A REVIEW ON NEW OFLOXACIN-FLUOROQUINOLONE ANALOGS: SYNTHESIS AND BIOLOGICAL EVALUATION OF DIFFERENT COMPOUNDS

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Abstract

Fluoroquinolones are important antimicrobial agents that have demonstrated activity against a wide range of Gram-positive and Gram-negative organisms and have proved useful against micro-organisms that are resistant to other antibacterial agents. Examples are Gatifloxacin, moxifloxacin, ofloxacin, pefloxacin, levofloxacin with new ones entering the market. This review is focused on fluoroquinolone especially ofloxacin. Quinolones, that all the clinically useful bear a fluorine group at the C-6 position and such quinolones are described as fluoroquinolones. They have a very good pharmacokinetic profiles and attain appreciable concentrations well above their MIC's in biological tissues.

The fluoroquinolones have been analyzed by various methods which have been described in different works of literature. This review needful in fluoroquinolone research and development, both in bulk and pharmaceutical dosage forms as well as their determination in biological fluids. However, increased prescribing has led to the recent emergence of fluoroquinolone-resistant bacteria which has necessitated the search of newer drugs with efficacy against resistant strains and efforts are on worldwide in this direction. The present review explores active ofloxacin derivatives having different biological activities published during the last 15 years, also critical aspects of structures concerning to biological activities. The present work gives the potential use of novel ofloxacin and fluoroquinolone derivatives.

Keywords: Fluoroquinolone analogs, ofloxacin analogs, synthesis, structures, biological activities, analytical studies.

Introduction

Fluoroquinolones are synthetic antibacterial agents are useful for the treatment of tubercular infections, respiratory infections, typhoid fever, urinary tract infections, respiratory infections, sexually transmitted diseases, bone joint infections, community-acquired pneumonia, acute bronchitis, and sinusitis. Fluoroquinolones contain two-ring structures in which there is a substitution at position *N*-1; most of the current agents have a carboxyl group at position 3, a keno group at position 4, a fluorine atom at position 6 and a nitrogen heterocyclic moiety at the C-7 position.[1] Piperazine at C-7 position has resulted in a wide range of clinically useful fluoroquinolone antibacterial agents, namely gemifloxacin norfloxacin,[102] ciprofloxacin, moxifloxacin, ofloxacin, pefloxacin,[91] gatifloxacin, levofloxacin. Fluoroquinolones with 7-piperazinyl moiety and 3-carboxylic acid, 5-position methylene bridge derivatives have been reported to possess potent antibacterial and other activities. Levofloxacin is a chiral version of the ofloxacin drug. Ofloxacin and norfloxacin behaved similarly in the effect of urine, serum, inoculum size, bactericidal properties. Ofloxacin activity is 5 times greater than that of pefloxacin and norfloxacin,[2]

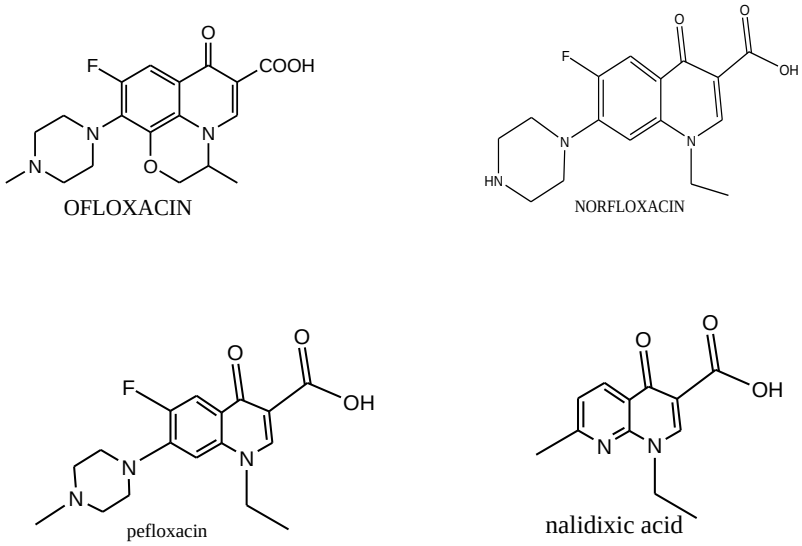

Fig: 1 fluoroquinolone derivatives.

Novel ofloxacin derivatives: Synthesis, antimycobacterial and toxicological evaluation

Thirty novel compounds were synthesized and have been evaluated for *In vitro* and *In vivo* antimycobacterial activities against MTB, MDR-TB, and MC2 and tested for the ability to inhibit the activity of DNA gyrase from mycobacteria. Among the synthesized compounds, the most active compound *In vitro* with MIC99 of 0.19lM and 0.09lM against MTB, MDR-TB. Animal models (*In vivo*) for the same

compounds decreased the bacterial load in lung and spleen tissues. Few Compounds are more active in the inhibiting activity of DNA gyrase with an IC50 of 10.0lg/ml. The results gave importance to develop novel oxazine quinolone analogs against mycobacterial infections. Biological activity: Anti-mycobacterial activity against MTB, MDR-TB, mc2, cytotoxic evaluation, phototoxic evaluation has been performed.[3]

Fig: 2 General structure of ofloxacin and fluoroquinolone derivatives.

Design, Synthesis and Antibacterial Evaluation of Novel Fluoroquinolone and its Derivatives

Gatifloxacin isomers are series of derivatives that were designed and synthesized and evaluated for their antibacterial activities(*In vitro)*. These results indicated that the tested compounds showed excellent MIC activity against staphylococcus epidermis, Klebsiella pneumonia. Compounds have been found to exhibit the most prominent activity against tested strains. From these results some tested compounds selected as a potential drug candidates for further evaluation.

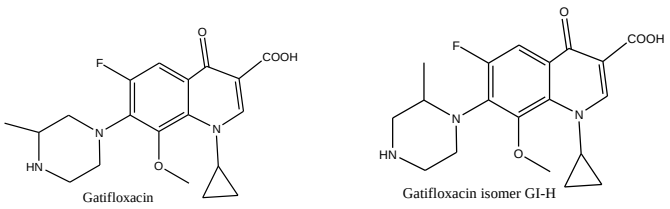

Fig: 3 Gatifloxacin derivatives.

Biological activity: antibacterial activity: synthesized compounds exhibit potent antibacterial activity against S.aureus, S.epidermidis, and E.coli, P.aeruginosa, K.pneumoniae. The MIC values were determined by comparing its isomer gatifloxacin as standard drug.[4]

Synthesis and antibacterial activity of novel levofloxacin derivatives containing a substituted thienylethyl moiety

The purpose of this study is Piperazinyl quinolones such as levofloxacin substitutes are important quinolone antimicrobials that are widely used in the treatment of various infectious diseases. We synthesized new compounds of levofloxacin derivatives and antibacterial activities have been studied.

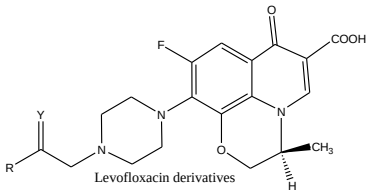

Fig: 4 levofloxacin derivatives.

R= thiophen-2-yl, thiophen-3-yl, 5-chloro thiophen-2-yl, 5-bromothiophen-2-yl. Y=O, NOH, $NOCH_3$, $NOCH_2Ph$.

Biological activity: Antibacterial activity: compounds were screened for their antibacterial, gram-positive bacteria and gram-negative bacteria by conventional agar dilution method reference drug levofloxacin, N-dimethyl levofloxacin. The MIC values were obtained reveals higher susceptibility for gram-positive and lower for gram-negative bacteria. The MIC values of ketones and oximes showed better activity than the standard drugs. Thus introduces structural features of levofloxacin analogues for development of the new drug in the field of anti-Gram-positive chemotherapy.[5]

Correlation between GyrA Substitutions and Moxifloxacin, Ofloxacin, Levofloxacin Cross-Resistance in Mycobacterium tuberculosis

The new fluoroquinolones moxifloxacin and levofloxacin are becoming more common drugs of tuberculosis treatment regimens. The critical concentrations for testing susceptibility of MTB to moxifloxacin and levofloxacin are not established. Also besides, the degree of cross-resistance between ofloxacin and new fluoroquinolones has not investigated properly. In this study, the MICs for moxifloxacin and levofloxacin and susceptibility to a critical concentration of ofloxacin were determined using the agar method for MTB (133 isolates). The mutations present within the gyrA QRDR compared with MICs, and the moxifloxacin and levofloxacin resistance level was dependent on the specific gyrA mutation. Substitutions resulted in low-level moxifloxacin resistance. Based on these results, a critical concentration of 1g/ml is suggested for levofloxacin and 0.5g/ml for moxifloxacin drug susceptibility testing by agar proportion.[6]

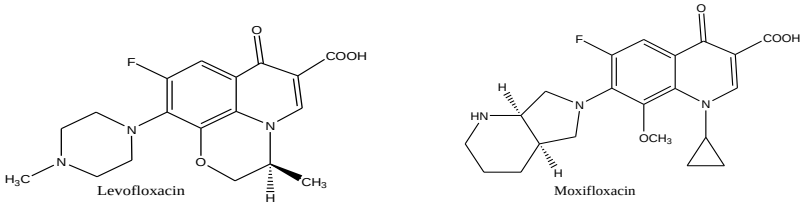

Fig:5 Levofloxacin and moxifloxacin structures.

Synthesis and anti-HIV activity of arylpiperazinyl fluoroquinolones: a new class of anti-HIV agents

Synthesis and anti-HIV activities of a new series of arylpiperazinyl fluoroquinolones are reported. In this study, the aryl substituents on the piperazine nitrogen were played an important role for the anti HIV-1 activity.[69] A few compounds exhibited potent anti-HIV activity and have been tested in infected cells. Biological activity: inhibitory activities of IC 50 and CC 50 has been calculated.[7]

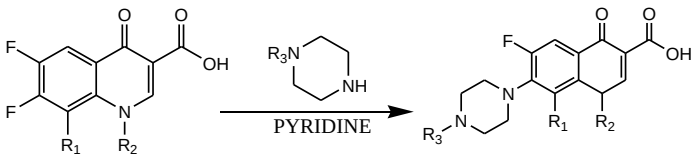

Fig:6 Synthesis of arylpiperazinyl fluoroquinolones.

Biological Activity and Synthetic Methodologies for the Preparation of Fluoroquinolones, a Class of Potent Antibacterial Agents

Different synthetic methodologies for the preparation of fluoroquinolones[68] and their biological properties have been studied. Fluoroquinolones have a wide spectrum of activity against Gram-positive, Gram-negative, mycobacterial organisms, anaerobes.

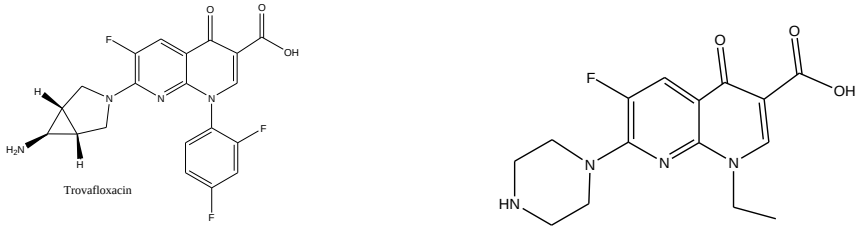

Fig:7 Trovafloxacin and Enoxacin[101] structure

Biological activity: Despite the antibacterial activity of fluoroquinolones, which also inhibits Mammalia topoisomerase-II as potential lead compounds in the development of anticancer drugs, they also showed great anti-HIV activity and inhibit the transcription of HIV-1. Trovafloxacin a fourth-generation fluoroquinolone also shown *In vitro* antimalarial activity.[8]

Novel Levofloxacin Derivatives as Potent Antibacterial Agent

A new series of fluoroquinolones derivatives of levofloxacin were synthesized and evaluated against Gram-positive and Gram-negative organisms. The results showed that compounds are strong antibacterial agents.

All the synthesized compounds showed good activities against Staphylococcus epidermidis, Staphylococcus aureus.

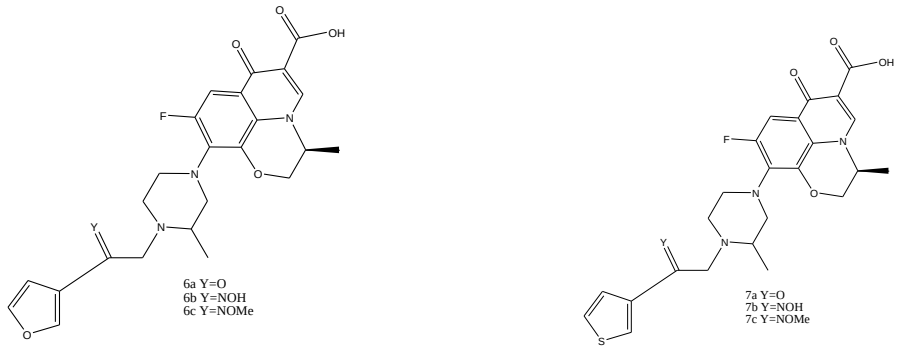

Fig:8 Levofloxacin derivatives.

Biological activity: the minimum inhibitory concentration (MIC) of compounds was determined by agar dilution method against four gram-negative and four gram-positive bacteria along with levofloxacin[65] for comparison. The MIC values were determined.[9]

Synthesis and Antibacterial Activities of Optically Active Ofloxacin

Two optically active isomers of ofloxacin (+-) were prepared by the use of their optically resolved synthetic intermediates. One of the isomers, (-)-ofloxacin is 8-128 times more potent in inhibiting the multiplication of gram-positive and gram-negative bacteria than the other, (+)-ofloxacin is approximately two times more active than the racemate. Biological activity: Anti-bacterial activity, the MIC of compounds determined by two-fold broth dilution method.[10]

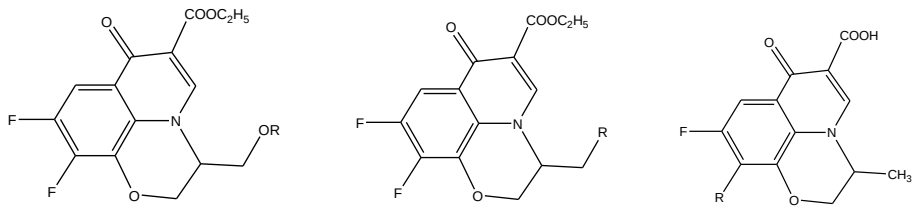

Fig:9 Ofloxacin derivatives.

Synthesis and anti-tubercular activity of ofloxacin derivatives

A new series of ofloxacin derivatives were prepared and screened for their antimycobacterial activity. Among the synthesized compounds, some derivatives exhibited significant antimycobacterial activity.

Biological activity: All synthesized compounds were evaluated for their antibacterial and antifungal and antimycobacterial activity.[11]

Fig:11 Ofloxacin different derivatives.

Synthesis and biological screening of fluoroquinolone antibiotic derivatives

Fluoroquinolone antibiotics play an important role in the medicinal field with so many pharmacological activities such as anti-fungal, anti-microbial, anti-viral, anti-HIV, anti-diabetic and anticancer activity[89]. The clinically useful drugs are used in the treatment of microbial infections and other activities encouraged the development of some more potent compounds. Finally, the preparation of Fluoroquinolone derivatives[88,90] and will have a positive impact on the Indian pharma industry by reducing the production cost, reducing production time and ecofriendly, when compared with the synthesis of antibiotic drugs by mannich reaction.

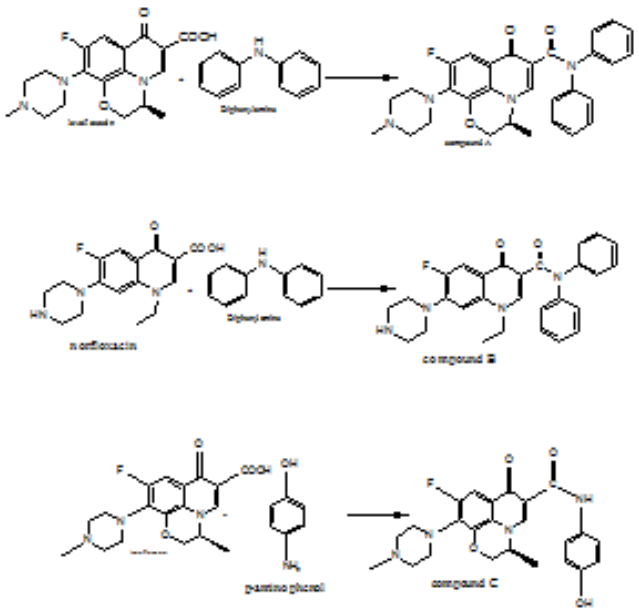

Fig: 12 Synthetic scheme of fluoroquinolones.

Biological activity: the antibiotic activity of synthesized compounds was determined by the zone of inhibition method. these drugs inhibits the bacterial action of a different organisms like B.Sbtilis, E.coli, K.Pneumonia, and S.aureus. The results of MIC of antibiotic was more for synthesized derivatives when compared to that of marketed derivatives based on the zone of inhibition values.[12]

Synthesis and Antibacterial Evaluation of new Ofloxacin-Chalcone derivatives Conjugates as Possible Mutual Prodrugs

To synthesize ofloxacin-chalcones conjugates as possible mutual prodrugs of enhanced antibacterial activity and evaluate activity against different strains of bacteria. Two chalcone derivatives have been synthesized using Claisen–Schmidt condensation of p-hydroxy acetophenone with p-fluorobenzaldehyde and p-bromobenzaldehyde using thionyl chloride, ethanol as a catalyst to obtain finally a fluorinated chalcone derivative and a brominated chalcone derivative. These synthesized chalcones were reacted with ofloxacin to obtain two possible mutual prodrugs that evaluated for its antibacterial activity against gram-positive and gram-negative bacteria in comparison with standard antibiotics: ofloxacin and ciprofloxacin using a disc diffusion method. FTIR Spectroscopy, elemental microanalysis, other properties have been used to find the structure of the synthesized compounds. These conjugates with ofloxacin were showed increased antibacterial activity in comparison with standard ofloxacin and ciprofloxacin using culture sensitivity test model on gram-positive and negative bacteria. Chalcones can enhance the activity of Fluoroquinolones.[13]

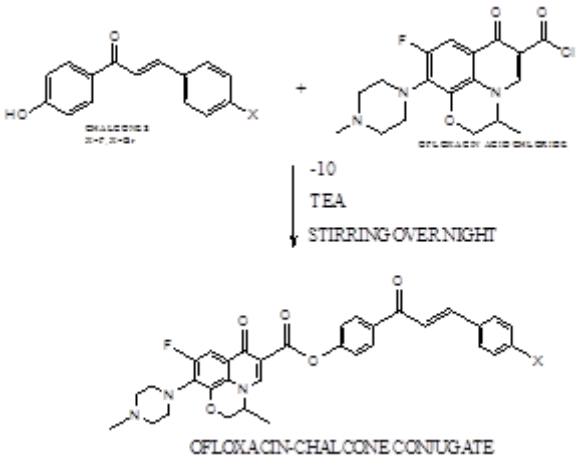

Fig: 13 Synthesis of ofloxacin-chalcone conjugate

Synthesis and biological evaluation of tetracyclic fluoroquinolones[86] as antibacterial and anticancer agents.

Synthesis of compounds was achieved via Stille arylation of 7-chloro-6-fluoro-8-nitro-4-oxoquinoline-3-carboxylate and a subsequent microwave-assisted phosphite-mediated Cadogan reaction. *In vitro* antimicrobial and antiproliferative activities tested for new compounds. The ability of compounds to inhibit the activity of DNA gyrase and topoisomerase IV was also investigated. The thieno isostere compound is the

most active antibacterial. The 9-fluoro derivative compound was most potent against MDR staphylococci. Some Compounds showed growth inhibition against MCF-7 breast tumor and A549 non-small cell lung cancer cells coupled with an absence of cytotoxicity toward normal human-dermfibroblasts. Compounds showed the most active anticancer against MCF-7 cells, with greater potency than ellipticine. Active compounds used as dual-acting for anticancer and antibacterial chemotherapeutics.

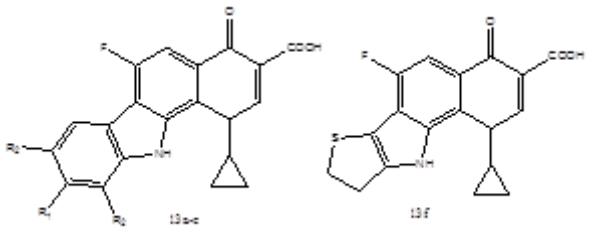

Fig: 14 Newly synthesized fluoroquinolones general structure.

Biological activity: the antimicrobial activity of novel heterocyclic compounds was assayed against 16 standard microorganisms of gram-positive, gram-negative bacteria, yeasts, molds. The inhibitory activity of compounds against bacteria is summarized with results obtained for commercial quinolones ciprofloxacin, levofloxacin, moxifloxacin, gemifloxacin used as reference drugs.[14]

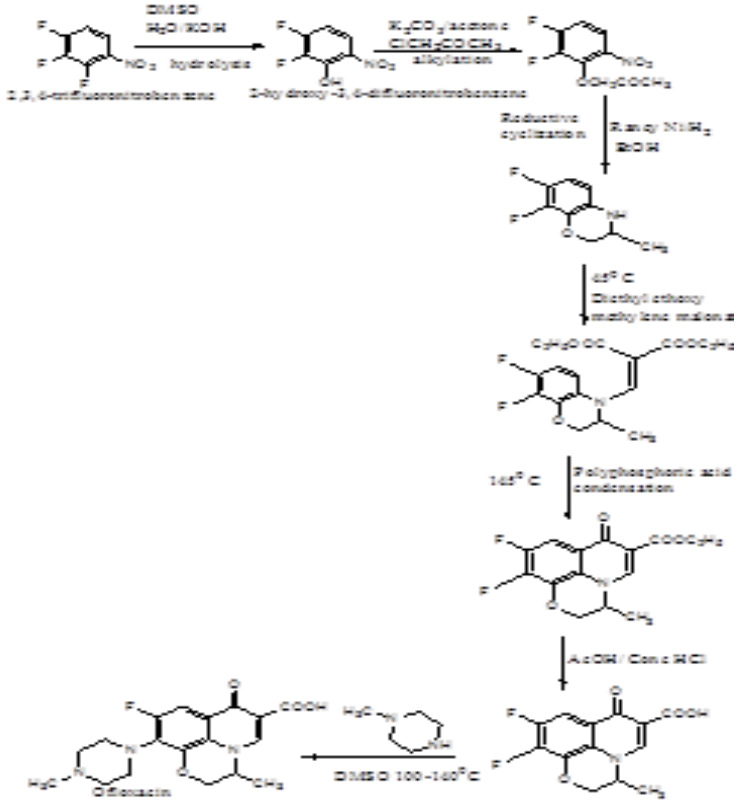

Fig:15 Synthesis of ofloxacin[15]

Synthesis, Characterization and Biological Evaluations of Ciprofloxacin Carboxamide Analogues.

The synthesis of various analogs of ciprofloxacin by introducing a new functional group at C-3 of the carboxylic group is esterified and then subjected to various aromatic amines. Structural analogs were confirmed by different techniques IR, $_1$H NMR, and mass spectrometry. Biological activity: antibacterial activity: the *In vitro* of 3-substituted carboxylic acid against gram-positive and gram-negative organisms along with parent drug. antifungal activity: ciprofloxacin is antimicrobial drug and inactive against fungi only moxifloxacin and gatifloxacin showed activity against Candida species, the antifungal activity was carried out against various fungi. From the result, we found that some compounds got enhanced activity against fusarium solanum, candida albicans.[16]

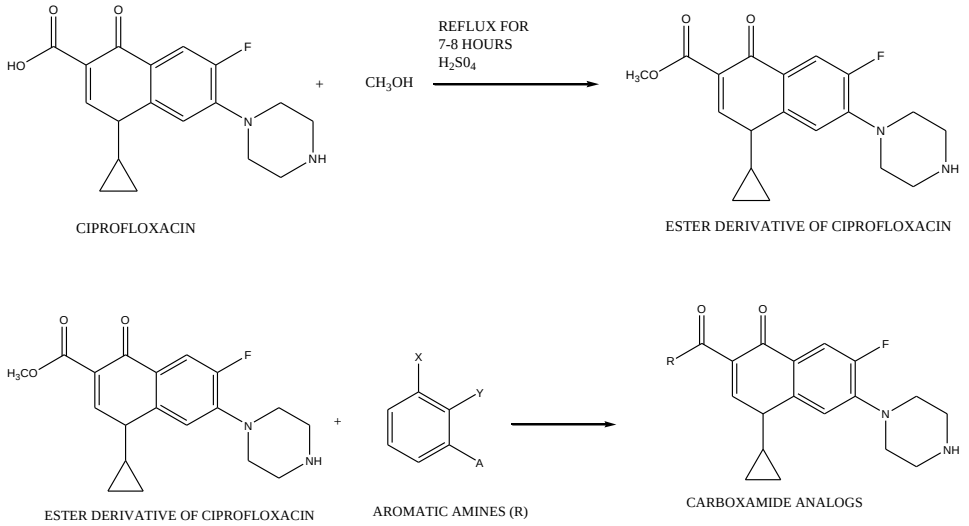

Fig:16 Synthetic pathway of ciprofloxacin derivatives

Compound 3a R=aniline.3b R=Toluidine.3c R=o-amino phenol, 3d R=3-amino phenol 3e R=phenylenediamine, 3f R=anisidine, 3g R=alpha napthylamine 3h R=phenyl hydrazine, 3i r=benzamide, 3j R=phthalimide.

Synthesis, characterization, antibacterial, antifungal, and immunomodulating activities of gatifloxacin derivatives.

Gatifloxacin is a synthetic broad-spectrum fluoroquinolone antibacterial agent with a 3-methyl piperazinyl-side chain at position 7 and a methoxy group at position 8 of the quinolone ring. Different gatifloxacin analogs were prepared. The piperazinyl ring was chosen for synthesizing series of derivatives. spectroscopic techniques such as IR, $_1$H NMR, EIMS developed for structure identification. These derivatives were compared with gatifloxacin, gemifloxacin, sparfloxacin. compound A proved very potent against Gram-

negative organisms, Pseudomonas aeruginosa, Shigella flexeneri, and Klebseilla pneumoniae, compounds A and C exhibited good antifungal activity compared to in-use quinolones. Biological activity: Antibacterial and antifungal activity was evaluated by the paper disc diffusion method. Antimicrobial activity was determined by calculating the percentage zone of inhibition taking gatifloxacin as standard. Screening of gatifloxacin and its derivatives using whole blood for chemiluminescence activity and screening for immune-modulating inhibitory properties has been done.[17]

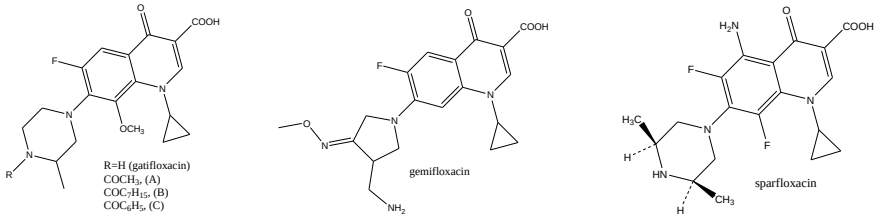

Fig:17 Structures of gatifloxacin and fluoroquinolone derivatives.

Synthesis, antibacterial, antifungal and anti-HIV activities of norfloxacin Mannich bases.

Norfloxacin mannich bases were synthesized by reacting with formaldehyde and several isatin derivatives. IR, $_1$H-NMR data and elemental analysis confirmed chemical structures. *In vitro* antimicrobial activity was done by the agar method against pathogenic bacteria, pathogenic fungi and anti-HIV activity[77-79] against replication of HIV-1 (III B) in MT-4 cells. Antibacterial efficacy (*In vivo*) of selected compounds was done by a mouse infection model. The observations showed very good activity against tested bacteria. All compounds are more active than norfloxacin[85] and MIC values were determined. Antifungal activity: all compounds exhibited significant antifungal activity/ all compounds are more potent than norfloxacin against the fungi tested when compared to clotrimazole. Anti-HIV activity: the compounds were evaluated for their inhibitory effect on the replication of HIV-1 in human MT-4 cells.[18]

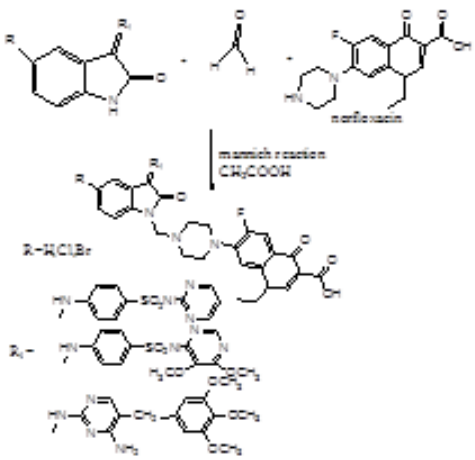

Fig:18 Scheme for norfloxacin mannich base derivatives.

Synthesis and Antiviral Studies of Novel N-Sulphonamido methyl piperazinyl Fluoroquinolones

Compounds were synthesized through modifying the N4 hydrogen of piperazine with formaldehyde and sulphonamides (Mannich base reactions). The synthesized compounds screened by spectral data. Biological activity: compounds applied to influenza A and B viruses replication was determined by cytopathic effect inhibition (CPE). Standard Ribavirin inhibits the replication of influenza A and B viruses. Compounds were tested for inhibitory effects against the replication of HIV-1 in MT-4 cells. The EC50 values of the compounds against the replication of HIV-1 were higher than the cytotoxic concentration, zidovudine used as standard drug.[19]

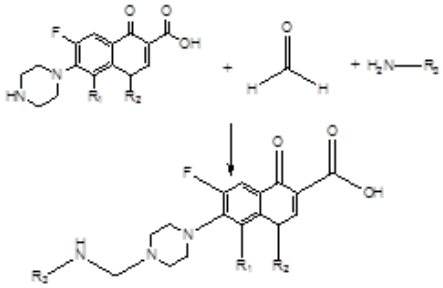

Fig:19 Scheme: synthesis of N-sulphonamidomethyl fluoroquinolones.

To synthesize the C-7 position of quinolone analogs of the main nucleus gives different derivatives with potent antimicrobial activity (*In vitro*).[20]Another aspect is the evaluation of a new series of fluoroquinolone derivatives clubbed with benzothiazole moeity has been described.[21] Triazolidine dione moieties with fluoroquinolones have been synthesized and proved to be cytotoxic agents *In vitro* particularly against cancer cell lines. Synthesized compounds showed less cytotoxicity than doxorubicin (standard) in cell lines. The best results were obtained for the compound 3a and 3b.[22] Ofloxacin UV analysis[23] has been determined. Ofloxacin Schiff bases[24] has been synthesized, performed studies on QRDR using docking studies. Anti-malarial activity[25] of ciprofloxacin and synthesized ciprofloxacin imines[26] and their metal complexes. Statistical analysis[27] done on ofloxacin derivatives.

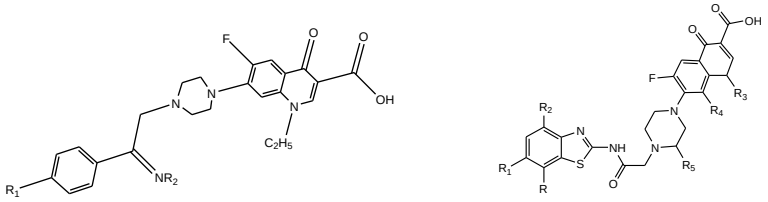

Figure:20 fluoroquinolone derivative and Benzothiazole clubbed fluoroquinolones

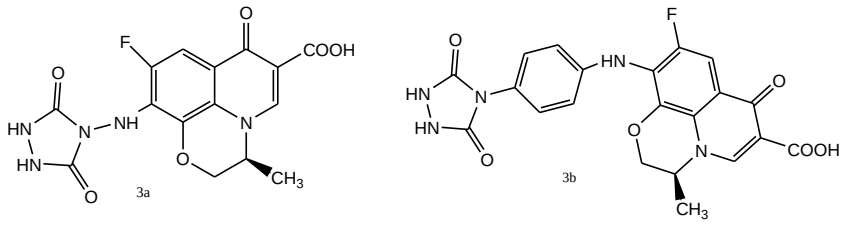

Fig:21 Compounds 7-substituted fluoroquinolones 3a and 3b

MTB crystal structure of DNA gyrase cleavage core and a fluoroquinolone-sensitized mutant and fluoroquinolone action were determined in complex with DNA .[93-100] The structures show that the intrinsically low susceptibility of Mtb to fluoroquinolones correlates with a reduction in contacts to the water shell of an associated magnesium ion, which bridges fluoroquinolone–gyrase interactions.[28] The activity of quinolone-carboxylic acids esters and new antiinfective agents against MDR-TB. Anti TB screening against H37Rv and clinically isolated strains of MTB. Several strains showed good MIC_{90} values.[29] The main biological target is DNA gyrase, topoisomerase-II encoded by gyrA and gyrB essential for DNA supercoil. The goal is to gather data of fluoroquinolones effective against TB, MDR-TB, XDR-TB, encourage the development of a new drugs.[30] fluoroquinolone-resistant multidrug-resistant and extensively drug-resistant tuberculosis. Delamanid, bedoquiline has been approved long back for the treatment of drug-resistant tuberculosis.[31]The early bactericidal activity of ciprofloxacin [83] was measured in some patients with positive-smear pulmonary tuberculosis by counting in sputum collections initial days of treatment. Groups of some patients were treated daily with graded doses of ciprofloxacin with or without drug along with 300 mg Isoniazid .[32,36]

The Antitubercular potential of quinoline, diamine, quinolone, fluoroquinolone, quinone, their possibility to be a future drug candidate, and latest information on the clinical status of some novel antitubercular compounds.[80-84] Compounds such as moxifloxacin are well tolerated and there is no adverse effect. Moxifloxacin and gatifloxacin shows cross-resistance to the currently used drugs.[33-34] The antitubercular activity also encompassed the bacteria in a non-replicating state (NRP-TB) with minimum inhibitory concentration values lower than those of the reference agent, moxifloxacin. Among the best compounds, properly substituted piperidine at the C-7 position, were active against single-drug-resistant (SDR-TB) Mtb strains, maintaining overall good potency also against ciprofloxacin-resistant Mtb. This study expands the body of SAR around antitubercular quinolones leading to reconsider the role played by the usual fluorine

atom at the C-6 position.[35-39] fluoroquinolones and quinolones cover the literature review from the past years with emphasis placed on new applications and mechanisms of the pharmacological action of quinolone derivatives.[40,103] Tuberculosis (TB)[76] has become a worldwide threat, mainly due to the emergence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains of Mycobacterium tuberculosis (Mtb). An organometallic ruthenium complex of quinolone antibacterial agent ofloxacin, RuCl, was isolated, and its crystal structure has been determined. Bidentate coordinated quinolone with the metal through the carbonyl ring and one of the carboxylic oxygen atoms. Interactions of the title complex with DNA were studied by spectroscopic methods and atomic force microscopy.[41-46] Novel potential antitubercular agents dihydroartemisinin–fluoroquinolone (DHA–FQ) conjugates were designed and conveniently synthesized. All the newly synthesized conjugates were well characterized and evaluated against different MTB strains (*In vitro*). The screening results showed DHA–FQ conjugates were active towards MTB H37Rv, and compounds exhibited the strongest inhibitory activity, which was comparable to the positive control Moxifloxacin and even stronger than Ofloxacin. Conjugates also displayed comparable activities against various clinically isolated sensitive and resistant MTB strains to Moxifloxacin. All target compounds possessed selective anti-MTB ability.[47-63] Levofloxacin[65] silver complexes are interesting for therapeutic purposes due to antifungal potential and antibacterial provided by the metal and fluoroquinolones. Some novel substituted 4-quinolone pyrazolidinedione derivatives[92,104]. The Purity of the compounds was checked by using TLC and elemental analysis. These compounds showed a antibacterial activity against S. aureus, B. subtilis, Klebsiella pneumonia and Proteus vulgaris and anti-inflammatory activity using *In vitro* testing methods compared to Ciprofloxacin, Amoxicillin, and Ibuprofen respectively.[66,67,70]

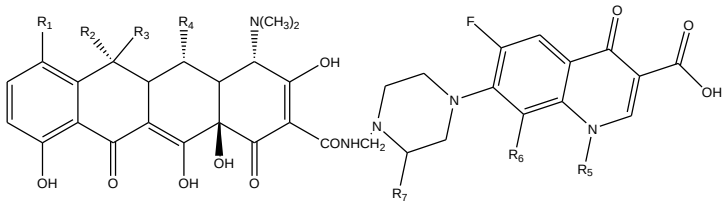

Fig-22 Tetracycline-fluoroquinolone structure[69]

The lead compound via the virtual screen in synthesized a series of analogs of compounds. Their primary anti-HIV properties against integrase reveal that the 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.[71-73]

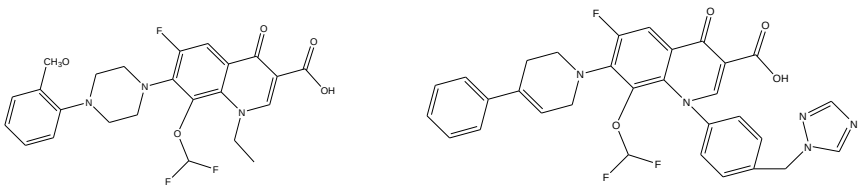

Fig:23 k-12, Inhibitor of herpes viruses.[74] and Anti HIV-fluoroquinolone.[75]

We focused on modification of the basic structure of ofloxacin by introducing new functionality at the C3 position. The structure of these derivatives was established by various analytical techniques i.e., IR, 1H-NMR, 13CNMR CHNS elemental analysis and mass spectrometry. The antibacterial activity of ofloxacin[64] and its derivatives against different Gram-positive and Gram-negative microorganisms was studied using a disk susceptibility method.[87]

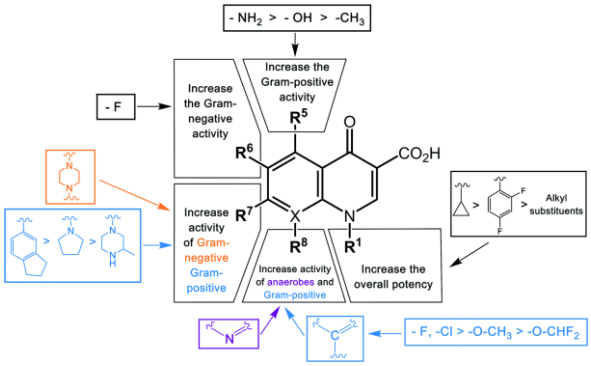

Fig:24 Structure activity relationship of quinolones.[104]

Synthesis and evaluation of Ofloxacin derivatives were carried out and evaluated for their anthelmintic activity. Synthesized ofloxacin derivatives were purified by using of Ethanol by recrystallization procedure and Characterized the molecules by analytical methods (TLC), Spectroscopic methods (FT-IR, Mass, and NMR). Insilico methods were adopted for synthetic derivatives by Molinspiration online software. Determined Evaluated anthelmintic activity of molecules of synthesized compounds by using Mebendazole as standard drug.[105]By searching google patents and USFDA, we found fluoroquinolone patents for ciprofloxacin, enrofloxacin, enoxacin, gatifloxacin, gemifloxacin, levofloxacin, lomefloxacin, moxifloxacin, norfloxacin, ofloxacin, sparfloxacin, trovafloxacin, difloxacin, cinofloxacin, pefloxacin, tosufloxacin, temafloxacin, fleroxacin, amifloxacin, binfloxacin, danofloxacin, marbofloxacin, ruflocaxin, and sarafloxacin.[106]

Conclusion

The present data reveal the several ofloxacin and fluoroquinolone derivatives and has been studied for different synthetic pathways, structures and biological activities & reactions have been studied. It becomes important to explore further of these molecules for the synthesis of high efficacy and less toxic, good therapeutic index molecules. This review will serve as research pathway in areas of anti-inflammatory, anti-mycobacterial infections, anti-influenza A, B virus, anthelmintic, antibacterial (*Invitro & In vivo*), some anaerobes, anti-fungal infections, anti-HIV-1, anti-HIV-2, anti-cancer studies, anti-malarial activities, cytotoxic and phototoxic evaluation anti-proliferative activities for the development of a new drug.

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Conflict of Interest:

Authors declare that there is no conflict of interest.

Abbrevations:

MIC=minimum inhibitory concentration, IC50=the half maximal inhibitory concentration, CC50= the 50% cytotoxic concentration, MTB=Mycobacterium tuberculosis, MDR-TB=multi-drug resistant Mycobacterium tuberculosis, MC2=Mycobacterium smegmatis

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