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Research article

Microwave assisted synthesis of 3-substituted aryl aminochloro flouroquinoline derivatives for antimicrobial activities

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ABSTRACT

Quinoline derivatives found to possess various activities such as antimicrobial, anti-tubercular, antifungal etc. 2,7-dichloro-6-fluoroquinoline-3-carbaldehyde was synthesized by treating 3-chloro-4-fluoroaniline with acetic anhydride, the intermediate (substituted acetanilide) obtained was further treated under microwave with dimethyl formamide /phosphorus oxychloride to get the desired product. Derivatives of 2,7-dichloro-6-fluoroquinoline-3- carbaldehyde [R-02] to [R-10] were synthesized by treating it with different anilines, oxindole and rhodanine. Synthesized derivatives were characterized by IR, 1HNMR and Mass spectra and evaluated for their antimicrobial properties. Antimicrobial study of these compounds shows that they have moderate activity against Gram-positive and Gram-negative strains of bacteria, but less than the standard drug (ciprofloxacin). Only [R-04] compound has slightly better activity than the standard drug (4µg/ml).

Keywords: Antimicrobial, Ciprofloxacin, Microwave 2,7-dichloro-6-fluoroquinoline-3-carbaldehyde.

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INTRODUCTION

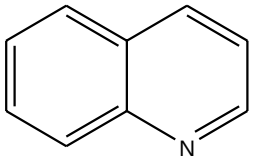
The biggest threat for human being is disease. To live a healthy life human civilization had tried various forms of medication. Thanks to inter disciplinary support which advanced the drug discovery process. Today we have come miles ahead from random and irrational drug discovery to systematic rational drug discovery. But it seems that microbes have advanced their biochemistry too. Medicines in-use are becoming inactive next day. So the threat is always there if existence of human life is concerned. To overcome this threat more than thousand molecules are getting synthesized and screened daily, but very few from them are getting the status of drug in the later stage. Development of heterocyclic chemistry and its successful application in the field of medicinal chemistry revolutionized the drug discovery process. Today more than 90% of drugs in use contain heterocyclic nucleus. Whether it is antibacterial penicillin, anti-tubercular isoniazid or antiviral acyclovir, all contain heterocyclic nucleus [1]. Development of natural chemistry and concept of derivatives has also advanced the drug discovery process. Today we have lot of newer drugs which are derivatives of less effective or more toxic parent drug. The best example is development of series of beta-lactam antibiotics.

A disease can't be classified like good or bad one. Whatever type of disease, it has to be treated with great care. But if difficulties in terms of prevention, treatment and complete cure are concerned then cancer, tuberculosis and viral diseases like Acquired Immune Deficiency Syndrome, Polio, Severe Acute Respiratory Syndrome and bacterial infections like typhoid, pneumonia, meningitis are still puzzling the human beings. Whatever advance meant we have achieved in drug development, wear still waiting for the one time effective treatment for the above said diseases.

Considering the above facts, synthesis and evaluation of some 3-substituted quinoline derivatives for their antimicrobial properties has been proposed.

Quinoline and its derivatives

It is a colourless hygroscopic liquid with molecular formula C_9H_7N.Quinoline is also known as, benzopyridine, benzo[b]pyridine, 1- benzazine and benzazine [2].Quinoline structure is known ever since 1908 and proved by total synthesis by Woodward and Doering in 1945.



QUINOLINE (Benzo[b]pyridine)

It was the structural model for all other anti-malarial quinoline derivatives. No any nucleus has been found to be as effective as quinoline against different strains of plasmodium protozoa. It was first isolated by Runge in 1834 from coal tar bases and subsequently, Gerhardt in 1842 obtained it from alkaline pyrolysis of cinchonine, an alkaloid related to quinoline [3].It was introduced for the treatment of urinary tract infections in 1963,the drugs containing quinolone nucleus includes oxolinicacid,norfloxacin, ciprofloxacin, etc. Since then, this nucleus of quinoline has been explored widely and its derivatives have been found to possess various activities ranging from anti-HIV, anti-malarial, anticancer, anticonvulsant, anti-tubercular, anti-infective and melanin concentrating hormone antagonists [4-15]. In 19th century the active principles of cinchona alkaloids, quinine and cinchonidine were isolated and purified. The formal synthesis of quinine by Woodward and Doering in 1944-1945 was a landmark in modern synthetic chemistry [16,17]. The first stereoselective total synthesis of quinine was recently reported by Stork and co-workers [18].

Quinoline and its analogs especially 4-quinolones have a number of advantages over other classes of antibacterial agents:-

Broad spectrum of activity

Well-absorbed orally

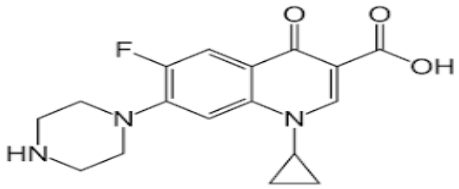
Well-distributed in tissues

Long serum half-lives

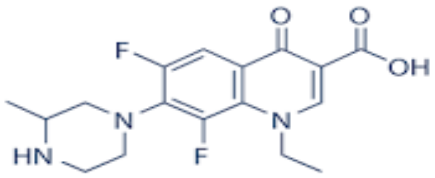
Minimal toxicity

Because of deep-tissue and cell penetration, they are useful for urinary tract infections, prostatitis, infections of the skin and bones, and penicillin-resistant sexually transmitted diseases. Some well-known quinolines antibiotics are norfloxacin, gatifloxacin, ciprofloxacin **(1)** and lomefloxacin**(2)** [19].

Figure 1: Gatifloxacin, Ciprofloxacin **(1)** and lomefloxacin**(2)**



(1)



(2)

The pelvic floor is made up of connective tissues and muscles that support vital organs like the bladder, colon, and internal reproductive systems during a variety of activities of daily living. Pelvic floor muscle insufficiency results in poor control over continence during various activities (like coughing and sneezing) which involves a rise in intra-abdominal pressure. Delayed muscle recruitment, reduced tonic activity, and muscle weakness are some common characteristics of pelvic floor sufficiency [1,2]. Factors like obesity, chronic coughing, heavy weightlifting, frequent constipation, parity, number of childbirth, presence of low back aches, and many other health conditions are found to be related to pelvic floor dysfunction (PFD) [3-5]. PFD is an umbrella term that includes urge incontinence, stress incontinence, overactive bladder, and organ prolapse. The functioning of the pelvic floor becomes more important among females due to its high prevalence [6]. The prevalence of PFD in various forms varies from 14.2% to 34.3% [7]. Data for the Indian population is not available, but studies reported that prevalence at the district level is around 21% among women [8]. The actual prevalence may be higher in different ethnicity as women consider PFD as a normal part of life, hence remaining unreported.

Pelvic floor functions in synergy with the rectus and transverse abdominis muscle to control continence by regulating intra-abdominal pressure [9]. These muscles along with erector spinae play a key role in stabilizing the spine during various functional activities and postures. Co-contraction of various global and local muscles is required to have better spinal stability. The spinal stability gets compromised in case of high Body mass index (BMI), which in turn reduces the postural control ability of erector spinae. Global muscles functions to transfer the load to the pelvis while local muscles are responsible for segmental stability [10-13]. Optimal spinal stability facilitates pelvic floor functioning by improving lumbopelvic rhythm. This function of pelvic floor with co-contraction of abdominal muscles becomes more challenging in gravity-dependent postures like standing. The lumbar posture affects muscle recruitment and its tone to regulate spinal stability[14]. Limited mobility, weakness of muscles, and laxity in ligaments supporting the spine results in a change in the normal curvature of the lumbar spine among menopausal women [15]. When this change in the lumbar spine becomes habitual, this not only affects the pattern of trunk muscle activation, but also the tonic activity of these muscle [16,17].

Study investigated the association between lumbar lordotic angle and spinal stability, but how spinal instability affects the trunk muscle activation remains unanswered [18]. Despite being the key stabilizer of the spine which in turns affects the lumbopelvic rhythm,

evidence finding the association between trunk muscle activity with variety of habitual lumbar curvature among post-menopausal women are still lacking. Few studies also investigated the role of trunk muscle coactivation during pelvic floor functioning [9], but this coactivation of trunk muscle in presence of different lumbar spine curvature in sagittal plane is still no studied. Where the present literature studied and identified the association between trunk muscle activation with voluntary adopted lumbar posture and with pelvic floor functioning separately, none of them identified this muscle activation and pelvic floor function with respect to different habitual lumbar posture. In this study we tried to identify this gap that, how the variety of habitual lumbar posture effects the tonic activity of rectus abdominis and erector spinae along with intravaginal pressure as a function of pelvic floor muscle in antigravity position while standing still and doing the task which raises intra-abdominal pressure post-menopausal women.

MATERIALS AND METHODS

Procedure For Synthesis of N-(3-Chloro-4-Fluorophenyl) acetamide

10 g (0.06 mol) of 3-chloro-4-fluoro-aniline was dissolved in 25 ml of glacial acetic acid in a 250ml round bottom flask. To this solution, added 12.5 ml of acetic anhydride and refluxed for thirty minutes, added 10 ml of cold water into the reaction mixture. Boiled the reaction mixture for additional five minutes to hydrolyze any un-reacted acetic anhydride .Cooled and poured with stirring into 75 ml of ice cold water. Washed the precipitate obtained with 25 ml of cold water, dried and recrystallized from ethanol[20].The melting point was found to be 95°C. The yield of acetanilide was 9g (90%).

Synthesis of 2,7-dicholoro-6-fluoroquinoline-3-carbaldehyde[R-01]

Phosho-oxychloride (0.5mol) was added drop wise with stirring to 0.3mol of DMF at 0°C.To this solution was added acetanilide (1mol) and after 5 minutes heated under microwave (Catalyst TATA-R) irradiation for1 hour at different level Table-1.The reaction mixture was poured into ice cold water and stirred for 30 min. The product was isolated and recrystallized from ethanol yield 94% M.P is120-122ºC.

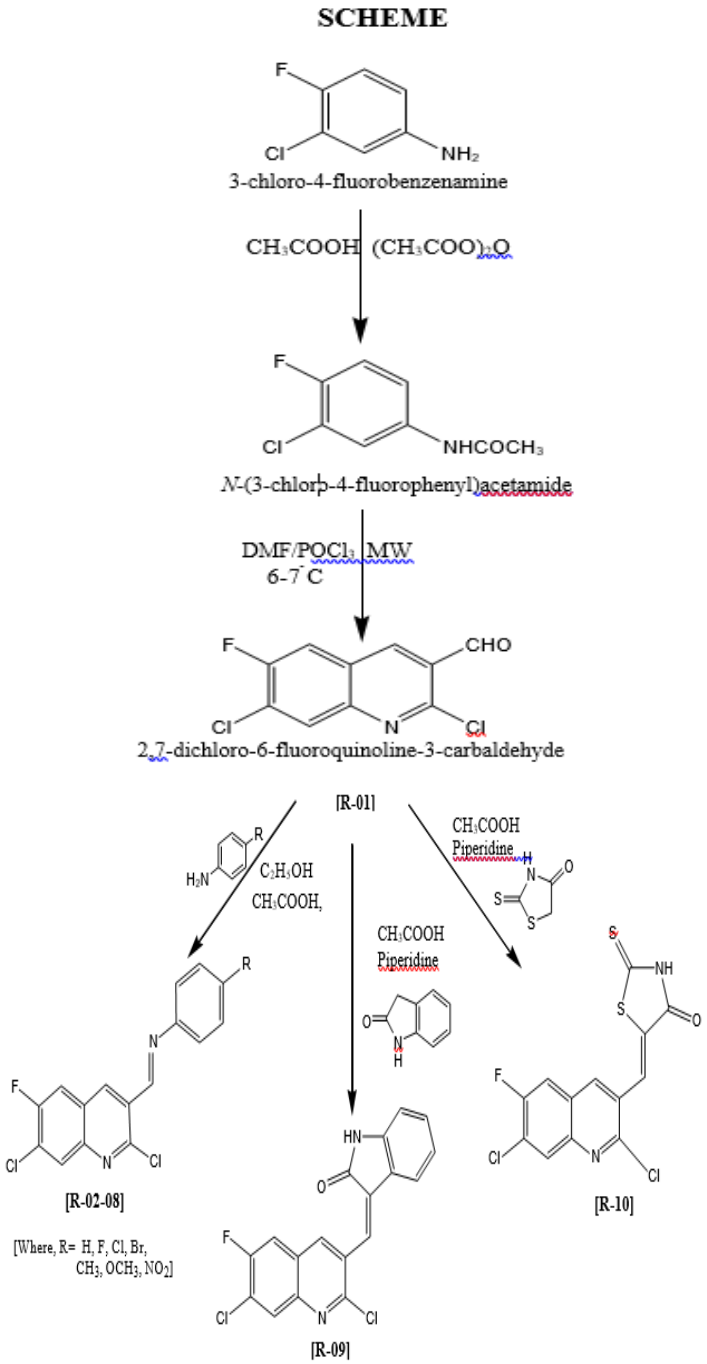
Synthesis of different (2,7-dicloro-6fluoroquiquinolin-3-yl) methylene)benzamine[R-02-08]

To a mixture of 2,7-dicholoro-6-fluoroquinoline-3-carbaldehyde [R-01] (0.5 mol) and Substituted aniline (0.5mol) and 1ml of glacial acetic acid were taken into round bottom flask containing 50 ml of ethanol. And refluxed till completion of the reaction as confirmed by TLC. The resulting product was recrystallized from ethanol.

Synthesis of (E)-5-((2,7-dichoro-6-fluoroquinolin-3-yl)methylene)-2-thioxothiazolidin-4-one[R-09-10]

To a 0.005(mol) solution of formyl quonoline in 50ml methanol, added 0.005(mol) of oxindole /2-thioxothiazolidine-4-one, 0.2 ml of piperidine and refluxed till completion of the reaction as confirmed by TLC. The resulting product was recrystallized from ethanol.

Figure 2: Resulting product



Biological evaluation

Anti-microbial activity

Preparation of stock solution

Stock solution of the synthesized compounds and standard drug (Ciprofloxacin obtained as a gift sample from Mahendra Labs Pvt Ltd., Bengaluru) used were prepared in dimethyl formamide taken in the concentration of 1µg/ml, 2µg/ml, 3µg/ml, 4 µg/ml for bacteria.

Cultures used

Standard cultures of *Bacillus subtilis, Staphylococcus Aureus,* and *Escherichia coli* species were obtained from Microbiology Lab, K.L.E.U. College of Pharmacy, Bangalore.

Table 1: Composition of nutrient agar media used for bacteria

Ingredients	Weight in gm.
Beef extract	1.50
Peptic digest of animal tissue	5.00
Yeast	1.50
Sodium chloride	5.00

Disc diffusion method

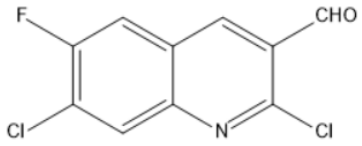
The petri dishes were washed thoroughly and sterilized in hot air oven at 170˚. 30 ml of sterile nutrient agar medium for bacteria was poured into sterile petri dishes and allowed to solidify. Thepetridisheswereincubatedat37˚for 24h to check for sterility. The medium was seeded with the organism by spread plate method using sterile cotton swabs and then placed the disc of Whatmann filter paper, pre-saturated with different dilutions of **(R-02, 03, 04, 05, 06, 07, 08, 09and R-10)** of synthesized compounds and a standard solution of ciprofloxacin on the agar media. The petri plateswereincubatedfor24hat 37˚Cand then the zones of inhibition were measured.

RESULTS & DISCUSSION

Chemistry

Results are summarized in the tables **[1-7].** 2,7-dichloro-6-fluoroquinoline-3-carbaldehyde [**R-1]** is a versatile starting material for the synthesis of number of proposed compounds **[R-02-10]**.Once the starting compound synthesized the different 3-substituted-quinolines were prepared by reacting the 2,7-dichloro-6-fluoroquinoline-3-carbaldehyde **[R-01]** with different reagents as per literature. The synthesized compounds were purified from suitable solvents. The infrared spectrum of 2,7-dichloro-6-fluoroquinoline-3-carbaldehyde **[R-01]** has shown the peaks at wavenumber3082.65(-CH,*ar.*),1671.02(>CO),1599.66(>C=N).1519.63(>C=C),1111.76(C-F) cm-^{1}. In ^{1}HNMR there were well resolved resonance peak at 9.61 (1H, -CH), 7.30-7.50 (3H, Ar-H) ppm. LCMS of the compound shows peak at244.9 (244.05). The IR spectra of 3-substituted quinoline derivatives **[R-02-10]** have shown peaks at wave number 3091.33-3053.73(-CH,*ar.*),2991.05-2917.77 (CH,*ali.*), 1745.26-1702.84(>CO),1654.52-1599.66(>C=N).1602.56-1525.42 (>C=C), 1129.33-1063.55(C-F)and1519.63cm-^{1} (NO_2). The ^{1}HNMR of the compound **[R-03]** shown well resolved resonance peak at 7.30-6.71(6H, Ar-H), 7.81(1H,-CH) ppm respectively. The ^{1}HNMR of the compound **[R-09]** has shown well resolved resonance peak at 7.34-6.52 (7H, Ar-H), 7.91(1H, -CH) and 12.90 (1H, -NH) ppm respectively. LCMS of compound**[R-02, 03, 05]**have shown peak at 244.90,353.10, and397.10respectively.

Figure 3: Physicochemical data for 2,7-dichloro-6-fluoroquinoline-3-carbaldehyde.

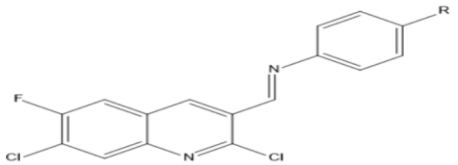


[R-01]

Table 2: Physicochemical data for 2,7-dichloro-6-fluoroquinoline-3-carbaldehyde.

CODE	M.F.	M.W. (gm)	M.P (˚C)	Rf VALUE
R-01	$C_{10}H_4Cl_2FNO$	244.05	223-25	0.63

Figure 4 : Physicochemical data for benzenamine derivatives.

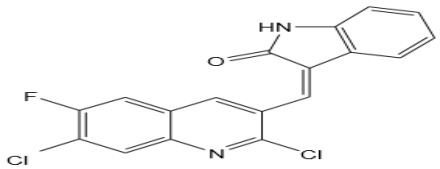


[R-02-08]

Table 3: Physicochemical data for benzenamine derivatives.

CODE	R	M.F.	M.W. (gm)	M.P. (˚C)	Rf value
R-02	H	$C_{16}H_9Cl_2FN_2$	319.16	268-70	0.72
R-03	Cl	$C_{16}H_8Cl_3FN_2$	353.61	232-34	0.68
R-04	F	$C_{16}H_8Cl_2F_2N_2$	337.15	272-75	0.44
R-05	Br	$C_{16}H_8BrCl_2FN_2$	398.06	241-43	0.86
R-06	NO_2	$C_{16}H_8Cl_2FN_2NO_2$	364.16	229-33	0.54
R-07	CH_3	$C_{17}H_{11}Cl_2FN_2$	333.19	280-82	0.66
R-08	OCH_3	$C_{17}H_{11}Cl_2FN_2O$	349.19	218-23	0.40

Figure 5: Physicochemical data for2-methylene-indoline-3-one derivative

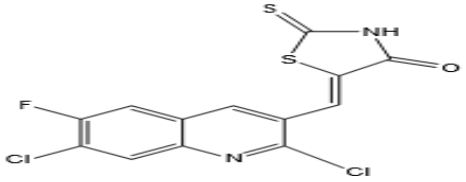


[R-09]

Table 4: Physicochemical data for2-methylene-indoline-3-one derivative

CODE	M.F.	M.W (gm)	M.P (˚C)	Rf VALUE
R-09	$C_{18}H_9Cl_2FN_2O$	359.18	266-68	0.48

Figure 6: Physicochemical data for2-thioxothiazolidin-4-one derivatives



[R-10]

Table 5: Physicochemical data for2-thioxothiazolidin-4-one derivatives

CODE	M.F.	M.W (gm)	M.P (˚C)	Rf VALUE
R-10	$C_{13}H_5Cl_2FN_2OS$	358.24	297-99	0.54

Table 6: IR-spectral data for synthesized compounds

Compound Code	IR(KBr disc) in cm-1
R-01	3082.65(-CH,*ar.*),1671.02(>CO),1599.66(>C=N), 1519.63(>C=C), 1111.76 (C-F).
R-02	3049.87(-CH,*ar.*),2917.77(CH,*ali.*),1596.77(>C=N),1549.52 (>C=C),1111.78(C-F).
R-03	3053.73(-CH,*ar.*),2971.77(CH,*ali.*),1745.26(>CO),1613.16 (>C=N),1581.34 (>C=C),1081.57 (C-F).
R-04	3051.80(-CH,*ar.*),2972.59(CH,*ali.*),1662.34(>CO),1623.77 (>C=N),1500.35 (>C=C),1263.15(C-F).
R-05	3057.58(-CH,*ar.*),2914.88(CH,*ali.*),1595.81(>C=N).1525.42 (>C=C),1063.55(C-F).
R-06	3062.41(-CH,*ar.*),2917.77(CH,*ali.*),1654.52(>C=N),1596.77 (>C=C),1519.63(NO_2),1063.55(C-F).
R-07	3059.51(-CH,*ar.*),2948.63(CH,*ali.*),1645.95(>C=N),1597.73 (>C=C),1086.69(C-F).
R-08	3059.51(-CH,*ar.*),2918.73(CH,*ali.*),1651.73(>C=N),1594.84 (>C=C),1094.40(C-F).
R-09	3054.69(-CH,*ar.*),2918.73(CH,*ali.*),1702.84(>CO),1633.41 (>C=N).1602.56 (>C=C),1129.12(C-F).
R-10	3091.33 (-CH, *ar.*), 2991.05(CH, *ali.*), 1745.26(>CO), 1617.98(>C=N),1123.33(C-F).

Table 7: Mass spectral data for synthesized compounds

Code	Observed Mass
R-01	244.90 (244.05)*
R-02	319.16(318.32)*
R-03	353.10 (353.61)*
R-04	337.15(336.18)*
R-05	397.10(398.06)*
R-06	364.16(364.85)*
R-07	333.19(332.59)*
R-08	349.19(348.10)*
R-09	359.18(359.10)*
R-10	358.24(359.12)*

Anti-microbial activity

The synthesized compounds were evaluated for their anti-bacterial activities[21] against *Bacillus subtilis*, *Staphylococcus aureus*, *and E. coli*. It was found that compound **[R-03], [R-04]** and **[R-08]** is showing zone of inhibition similar to standard drug Ciprofloxacin against *Bacillus subtilis*at4µg/ml concentration. None of the compound is showing activity against, S. aureus, and E. coli similar to standard ciprofloxacin. Based on activity result it was found that chlorine at 4th position of the amine ring is essential for activity. Compound without halogen is not active against any type of bacterial strains **[R-02]**. Replacement of benzamine group from 3rd position of the quinoline ring by groups like oxindole and oxothiazolidinone leads to loss in activity **[R-09-10]**.

The compounds **(R-02, 03, 04, 05, 06, 07, 08, 09 and R-10)** were subjected to antimicrobial evaluation. The antimicrobial activity as calculated by the zones of inhibition against *B. subtilis*, *S.aureus* and *E.coli* are given in the Tables **8-10** and Figures **10-15**.

Table 8:^{1}HNMR-Spectraldata for synthesized compounds

Code	Chemical shift & nature of Proton (δ ppm)
R-01	9.61 (1H, -CHO), 7.30-7.50 (3H, quinolone).
R-02	9.31 (1H, aldimine), 7.20-7.40 (3H, quinolone).
R-03	7.30-6.71 (6H, Ar-H), 7.81(1H,-CH).
R-04	8.78 (1H, aldimine), 8.05-7.68 (3H, quinolone),7.31-7.24(4H, benzene),
R-05	9.11 (1H, aldimine), 9.28-7.33 (3H quinolone), 7.91-6.92(4H, benzene).
R-06	9.14(1H, aldimine), 9.28-7.31(3H quinolone), 7.99-7.37 (4H, benzene).
R-07	9.13 (1H,aldimine), 9.27-7.33 (3H quinolone), 7.30-6.82 (4H, benzene), 2.21 (3H,-CH_3).
R-08	9.12(1H,-CH aldimine), 9.28-7.33(3H, quinolone).
R-09	12.90 (1H, -NH), 7.91(1H, -CH), 7.34-6.52 (7H, Ar-H),
R-10	9.12 (1H aldimine), 9.28-7.33, (3H quinolone), 7.22-6.58 (4H, benzene), 3.92 (3H, O-CH_3).

Table 9: Antimicrobial activity of the synthesized compounds against B.subtilis

Compound name	Conc. µg/ml	Zone of inhibition (mm)	Compound name	Conc. µg/ml	Zone of inhibition (mm)
Ciprofloxacin	1	None	R-06	1	None
	2	None		2	6
	3	None		3	8
	4	12		4	9
R-02	1	None	R-07	1	10
	2	None		2	10
	3	None		3	10
	4	6		4	11
R-03	1	6	R-08	1	10
	2	12		2	10
	3	12		3	12
	4	12		4	11
R-04	1	10	R-09	1	6
	2	11		2	6
	3	11		3	8
	4	13		4	10
R-05	1	7	R-10	1	None
	2	11		2	None
	3	11		3	8
	4	11		4	10

Figure 10: Ciprofloxacin showing zone of inhibition activity against E-coli at four different concentration

Figure 11: R-02 showing zone of inhibition activity against *E-coli* at four different concentration

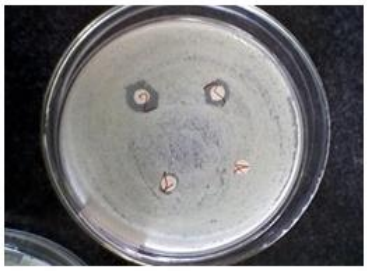


Figure 12: R-03 showing zone of inhibition activity against *B.subtilis* at four different concentration

Figure 13: R-04 showing zone of inhibition activity against *B.subtilis* at four different concentration

Figure 14: R-09 showing zone of inhibition activity against *E-coli* at four different concentration

Figure 15: R-10 showing zone of inhibition activity Against *S.aureus* at four different concentration

Table 10: Anti-microbial activity of the synthesized compounds against *S.aureus*

Compound name	Conc. µg/ml	Zone of inhibition (mm)	Compound name	Conc.µg/ml	Zone of inhibition (mm)
Ciprofloxacin	1	11	R-06	1	11
	2	12		2	12
	3	13		3	12
	4	13		4	12
R-02	1	6	R-07	1	6
	2	none		2	6
	3	8		3	10
	4	10		4	11
R-03	1	6	R-08	1	6
	2	10		2	8
	3	11		3	10
	4	11		4	11
R-04	1	5	R-09	1	6
	2	5		2	6
	3	6		3	8
	4	11		4	10
R-05	1	11	R-10	1	None
	2	11		2	6
	3	12		3	10
	4	12		4	10

Table-11: Anti-microbial activity of the synthesized compounds against *E.coli*

Compound name	Conc. µg/ml	Zone of inhibition (mm)	Compound name	Conc.µg/ml	Zone of inhibition (mm)
Ciprofloxacin	1	11	R-06	1	None
	2	19		2	None
	3	19		3	6
	4	21		4	8
R-02	1	6	R-07	1	10
	2	None		2	15
	3	6		3	15
	4	8		4	15
R-03	1	None	R-08	1	None
	2	None		2	None
	3	6		3	None
	4	8		4	6
R-04	1	None	R-09	1	None
	2	None		2	None
	3	8		3	None
	4	10		4	10
R-05	1	None	R-10	1	None
	2	None		2	6
	3	10		3	11
	4	11		4	12

CONCLUSION

The present work, which has undertaken is bonafied and novel for the synthesis of 2, 7-dichloro-6 -fluoroquinoline- 3-carbaldehyde derivatives. In this view we have made an attempt in reviewing the literature on 2,7-dichloro-6-fluoroquinoline-3-carbaldehyde for their medicinal significance with help of chemical abstract, journals and internet sites.2,7-dichloro-6-fluoroquinoline-3-carbaldehyde was synthesized with the help of microwave to reduce the solvent consumption as well as reaction time as compared to conventional method. Nine derivatives were synthesized with the standard chemicals and procedure. The synthesized derivatives were tested for the preliminary tests, physical constant sand TLC etc. The structure of final derivatives was confirmedy IR, ^{1}HNMR and Mass spectra. All synthesized compounds were evaluated for anti-bacterial activity against *Bacillus subtilis, Staphylococcus aureus,* and *E. coli.* Compound R-03 and R-08 shows similar activity as that of standard ciprofloxacin drug at 2,3,4 µg/ml while R-04 shows slightly better activity than that of standard drug.[R-04]shows better activity against Gram positive bacteria. Compound [R-03] to [R-10] has shown mild activity against Gram negative bacteria when compared with standard ciprofloxacin.

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Conflict of interest

There are no conflict of interest from all the authors

REFERENCES

1. Patel AS, Shah UA, Joshi HV,et al, 2022. Design, synthesis and biological screening of novel heterocyclic ring derivatives as antibacterial agents. Journal of medical pharmaceutical and allied sciences. 11(2), Pages – 4650 – 4656. Doi: 10.55522/jmpas.V11 I2.2623.

2. Jain S, Chandra V, Jain PK, et al, 2019. Comprehensive review on current developments of quinoline-based anticancer agents.Arabian Journal of Chemistry, 12(8), Pages -4920-4946. doi.org/10.1016/j.arabjc.2016.10.009.

3. Bansal RK, 2005.Text book of heterocyclic chemistry (4thedition).NewAgePublishers, Pages-326-328.

4. Benard C, Zovhin F, 2004.Linker modified quinoline derivatives targeting HIV- 1integrase: synthesis and biological activity. Bioorganic Med. Chem. Lett.14,Pages -2473-2476.Doi: doi.org /10.1016/j.bmcl.2004.03.005

5. Mehanna, SA, Abraham DJ Ed, 2003. Rationale of design of anti HIV Drugs. Burgers medicinal.(6th edition)John Wiley and Sons,Pages -457-459.Doi: doi.org/10.1002/0471266949.bmc084

6. Divo A, Sartorelli AC, Patton CL,et al, 1998.Activity of fluoroquinolines antibiotics against plasmodium falciparum.in-vitro Antimicrobial Agents Chemotherapy.32(8),Pages-1182-1186.Doi: doi.org/ 10.1128/aac.32.8.1182.

7. Gorlitzer K, Gabriel B, Jomaa H, et al, 2006. Thieno(3,2-c)quinoline -4yl-amines:Synthesis and investigations of activity against malaria.Pharmazie.61(4) ,Pages-901-907.

8. Khanfaruk MO, Levi SM, Takwani LB, et al, 2007. Synthesis of isoquincilidine analogs of chloroquin: antimalarial and antileishmanial activity.Bioorganic Med. Chem. Lett.15, Pages-3919-3925.Doi: doi.org/ 10.1016/j.bmc.2006.11.024.

9. Zhao YL, Chen YL, Tzeng CC, et al, 2005. Synthesis and cytotoxicity evaluation of certain 4-(phenylamino)-furo-(2,3-b)quinoline and 2-(furan-2-yl)-4-(phenylamino)quinoline derivatives.Chem Biodivers.2(2) ,Pages-205-214. Doi:

doi.org/10. 1002/cbdv.200590003.

10. Sun XY, Jin YZ, Li FN, et al, 2006. Synthesis of 8-alkoxy-4,5dihydro-(1,2,4)triazole(4,3-a)quinoline-1-ones and evaluation of their anticonvulsant properties, Arch PharmRes,29(12) ,Pages-1080-1085.Doi: doi.org/10.1007/BF02969295.

11. Xie ZF, Chai KY, Piao HR,et al ,2005. Synthesis and anticonvulsant activity of 7-alkoxyl-4,5 dihydro-(1,2,4)triazole (4,3-a) quinoline. Bioorganic Med. Chem, Pages-4803-4805.Doi: doi. org/10.1016/j.bmcl.2005.07.051.

12. Aubry A, Pan XS, Fisher M, et al, 2004. Mycobacterium tuberculosis DNA gyrase: Integrase with quinolones and correlation with antimycobacterial drug Activity. Antimicrobial Agents Chemotherapy, 48(4) Pages-1281-1288.doi.org/10.1128 /AAC.48.4.1281-1288.2004.

13. Nayyar A, Monga V, Malde A,et al ,2007. Synthesis and antitubercular activity and 3D-QSAR study of 4-(admantan-1-yl)-2- subustituted quinolines. Bioorganic Med. Chem. 15(2), Pages-626-640.doi.org/10.1016/j.bmc.2006.10.064.

14. Zhu XY, Mardenborough LG, Li S, et al, 2007. Synthesis and evaluation of isosters of N-methyl indole [3,2-b]-quinoline (cryptolepine) as new anti-infective agents. Bioorganic Med. Chem. 15,Pages-686-695.doi.org/10.1016/j.bmc.2006.10.062.

15. Souers A, Wodka D, Gao J, et al, 2004. Synthesis and evaluation of 2-amino-8-alkoxy quinolines as MCHr1 antagonist. Part 1. Bioorganic Med. Chem.Lett.14,Pages-4873-4877.doi.org/10. 1016/j.bmcl.2004.07.032.

16. Jarcho S.1993.Quinine's Predecessor Francesco Torti and the Early History of Cinchona.JohnsHopkins University Press, Baltimore: Pages-347-348. Doi: Doi.org/10.1017/S002572 7300 036759.

17. Woodward RB, Doering WE, 1945. Synthesis of quinoline analogues. J Am Chem Soc.67, Pages-860-874.Doi: doi.org/10. 1021 /ja01221a051.

18. Woodward RB, Doering WE, 1944.Synthesis, characterization and biological evaluation of of novel quinoline. J Am Chem Soc, 66, Pages-849.

19. Stork G, Niu D, Fujimoto A, et al, 2001. Synthesis and biological evaluation of new stereoselective analogues of quinine. J Am Chem Soc.123, Pages-3239-3242.Doi: doi.org/10. 1021/ja004325r.

20. Rizvi SUF, Siddiqui HL, Parvez M, 2010. Antimicrobial and antileishmanial studies of novel (2E)-3-(2-chloro-6-methyl/methoxyquinolin-3-yl)-1-(Aryl) prop-2-en-1-ones.Chem Pharm Bull.58(3), Pages-301-306.Doi: doi.org/10.1248/cpb.58. 301.

21. Bandigari P, Dongamanti A.2021. Purification, extraction of semecarpus anacardium by traditional method and evaluation of antibacterial activity. Journal of medical pharmaceutical and allied sciences. 10(5), Pages-3633-3635. Doi: 10.22270/ jmpas. V10I5.1430.

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