IJNRD.ORG ISSN : 2456-4184

INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG

An International Open Access, Peer-reviewed, Refereed Journal

SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF NOVEL 1,2-DIHYDROQUINOLINE BENZAMIDE DERIVATIVES

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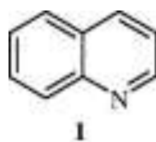
❖ **ABSTRACT:**

Quinoline or 1-aza-naphthalene is a weak tertiary base. Quinoline ring has been found to possess antimalarial, anti-bacterial, antifungal, anthelmintic, cardiotonic, anticonvulsant, anti-inflammatory, and analgesic activity. Quinoline not only has a wide range of biological and pharmacological activities but there are several established protocols for the synthesis of this ring. The present synthetic strategy is aimed towards the synthesis of benzamide containing1,2-dihydroquinoline derivatives [6a-h]. The synthetic route for the preparation is based on the transformation of 3-hydroxy Acetanilide into intermediate (2) followed by intermediate (3). All these synthesize compounds were tested for their antibacterial and anti-inflammatory activity.

❖ INTRODUCTION:

Quinoline [1] or 1-aza-napthalene or benzo[b]pyridine is nitrogen containing heterocyclic aromatic compound. It has a molecular formula of C9H7N and its molecular weight is 129.16. The logP value is 2.04 and has an acidic pKb of 4.85 and a basic pKa of 9.5. Quinoline is a weak tertiary base. It can form salt with acids and displays reactions similar to those of pyridine and benzene. It shows both electrophilic and nucleophilic substitution reactions. It is nontoxic to humans on oral absorption and inhalation.



Quinoline nucleus occurs in several natural compounds (Cinchona Alkaloids) and pharmacologically active substances displaying a broad range of biological activity. Quinoline has been found to possess antimalarial, anti-bacterial, antifungal, anthelmintic, cardiotonic, anticonvulsant, anti-inflammatory, and analgesic activity.

Importance of Quinoline:

Quinoline is a heterocyclic base and was first isolated in 1834 by Runge [1] from coal tar and he named it as Leukol. Later in 1842 Gerhardt [2] isolated it by heating the alkaloid cinchonine with alkali and named as quinoline. Large numbers of quinoline derivatives have been isolated from petroleum products [3]. Certain quinoline substances derived from natural or synthetic origin find significant use in the field of medicinal chemistry. Quinoline motifs are widely used as bioactive agents [4-7]. These heterocycles are used in the preparation of virucides, biocides, alkaloids, rubber chemicals and fragrant substances [8]. In addition, these compounds are used in the chemistry of metal catalysts of transition elements for polymerization process and luminescence properties [9]. Quinoline derivatives are used at refineries in the form of antifoaming agents [10]. Therefore, great interest has been created among synthetic organic and medicinal chemists for the synthesis of quinolines.

❖ MATERIALS AND METHODS:

1. Experimental Procedure

- Room temperature reactions mentioned ranges between 15-35°C (throughout the year). For low temperature reactions an ice-bath with sodium chloride (0°C) was used. Magnetically stirred oil bath (or) hotplate was used for high temperature reactions.
- Melting point of solid compounds range was determined in open capillary tubes using a hot stage apparatus.
- Progress of the reactions was monitored by TLC using Merck silica gel 60 F_{254} precoated on aluminium backed plates. TLC plates were visualized with ultraviolet light or iodine vapors or by staining with 2%

aqueous potassium permanganate solution.

- Silica gel (60-120 mesh) or neutral alumina was used for purification of synthesized compounds.
- The spectra were recorded using JASCO FTIR-4100 spectrophotometer as KBr disc.
- The ^{1}H and ^{13}CNMR spectra were recorded on Bruker model avance II (399.65 MHz, ^{1}H NMR) and Bruker model avance II (100.50 MHz, ^{13}C NMR) spectrometers using deuteriated solvents ($CDCl_3$& DMSO-d_6) and Tetramethylsilane (TMS) as an internal standard. The chemical shift values were expressed in δ ppm in both ^{1}H NMRand ^{13}C NMRspectra.
- LC-MS was recorded using Waters Alliance 2795 separations module and Waters Micro mass LCT mass detector.
- Elemental analysis (C, H and N) was performed on Elementarvario MICRO cube.

I. Step-1: Synthesis of 3-hydroxy Acetanilide [1]

3-aminophenol (0.11 mol, 25g) was dissolved in acetic anhydride (80 mL) and the reaction mixture was stirred at 60°C for 8 h at room temperature under nitrogen atmosphere. After completion of the reaction, the excess acetic anhydride was removed under reduced pressure; the residue was dissolved in methylene dichloride (MDC). The organic layer was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated to obtain compound (1). LCMS: 152 (M+1), MP: 152 °C. Yield: 82%.

II. Step-2: Synthesis of N-(4-methyl-2-oxo-2H-chromen-7-yl) acetamide[2]

A mixture of 3- hydroxy acetanilide (metacetamol) (0.1 mol, 15.1g) and ethyl acetoacetate (0.1 mol) with 70% sulphuric acid (50 mL) was heated carefully for 5 h. The resulting solution was cooled and poured over crushed ice (250 g). The crude product was filtered off and washed repeatedly with water, dried and recrystallized from hot water to result in title compound (3). LCMS: 205 (M+1), MP: 243 °C. Yield: 62%.

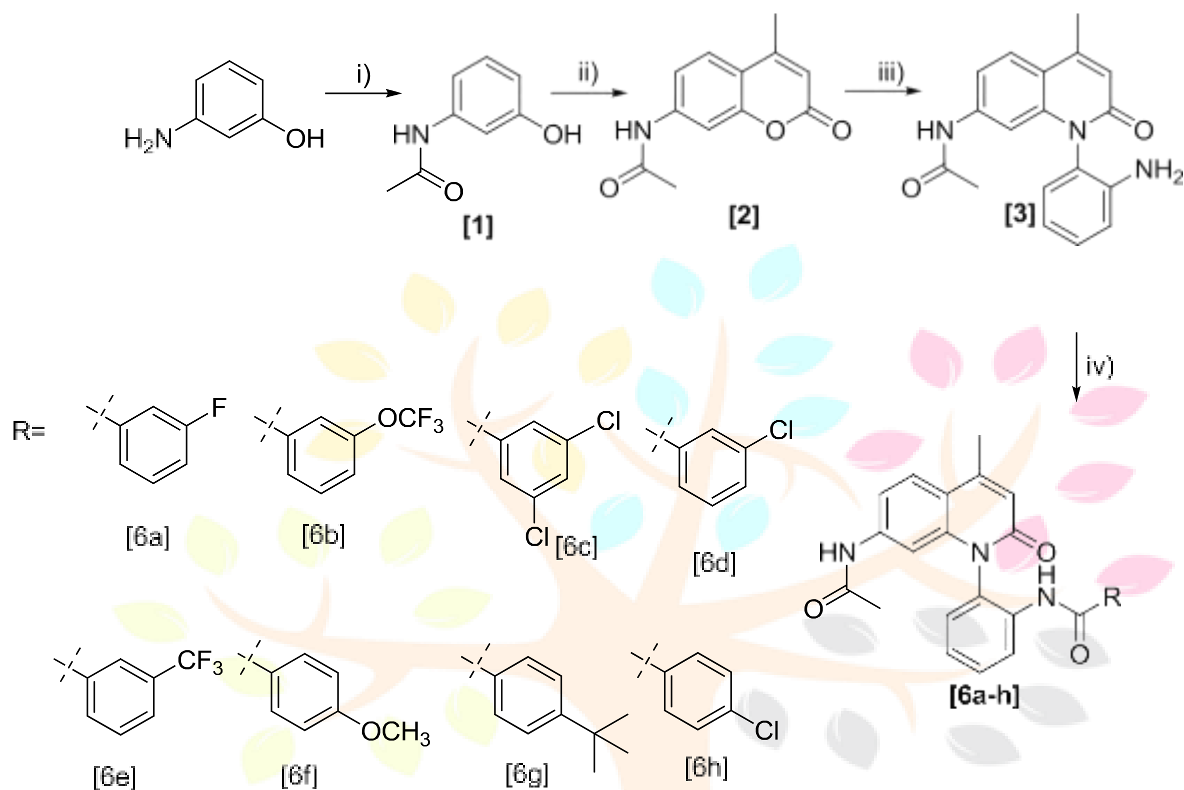
III. Step-3: Synthesis of N-[1-(2-aminophenyl)-4-methyl-2-oxo-1,2-dihydroquinolin-7-yl]acetamide [3]

A mixture of N-(4-methyl-2-oxo-2H-chromen-7-yl) acetamide (0.01 mol, 2.17g), o- phenylenediamine (0.01 mol, 1.08g) and sodium acetate (5 g) in glacial acetic acid (15 mL) was refluxed for 8 h and cooled. The separated solid was filtered and recrystallized from methanol: water (1:2) to give title compound (3). LCMS: 237.8 (M+1), MP: 285 °C. Yield: 70%.

IV. Step-4: Synthesis of 1,2-dihydroquinoline benzamides [6a-h]

Equimolar quantities of compound [4] (0.5 g, 0.001 mol) and different substituted benzoyl chlorides (0.001 mol) such as 3-fluoro, 3-methoxy and 3,5-dichloro benzoyl chlorides, K_2CO_3 (0.003 moles, 0.57 g), were stirred in dry ACN (10 mL) under nitrogen at room temperature for 10 h. The reaction was

monitored by TLC and the reaction mixture was filtered. The organic ACN phase was dried using anhydrous Na_2SO_4 and evaporated. The residue was purified by column chromatography using petroleum ether: ethyl acetate as eluent (8:2) to get benzamide dihydroquinoline nucleus (6a-h) in good yield (scheme 4.1).



[Scheme 4.1]

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Table: 1 Structure and Physical characterization data of 1,2-dihydroquinoline Benzamides [6a-h]

Entry	Structure	Mol Formula (Mol Wt.)	Yield (%)	Melting Point (°C)
6a		$C_{25}H_{20}N_3O_3F$ (429.44)	72	221-223
6b		$C_{26}H_{20}N_3O_4F_3$ (495.44)	72	241-242
6c		$C_{25}H_{19}N_3O_3Cl_2$ (480.34)	75	251-253
6d		$C_{25}H_{20}N_3O_3Cl$ (445.90)	280	218-219
6e		$C_{26}H_{20}F_3N_3O_3$ (479.45)	70	216-218
6f		$C_{26}H_{23}N_3O_4$ (441.48)	85	251-253
6g		$C_{29}H_{29}N_3O_3$ (467.56)	91	222-223
6h		$C_{25}H_{30}ClN_3O_3$ (445.90)	85	231-232

Table 2: Spectral data of synthesized compounds

Comp.	Spectral Data
6a	**IR: ν_{max}/cm^{-1}:** 3340 (N-H), 2228 (CN), 1698 (CO), 1342–1140 (CF stretching). **^{1}H-NMR ($CDCl_3$) δ:** 9.32 (s, 1H, NH), 7.88-7.86 (d, *J* = 8.7 Hz, 1H, Ar-H),7.85-7.77 (d, *J* = 1.9 Hz, 1H, Ar-H), 7.78-7.76 (d, *J* = 8.3 Hz, 1H, Ar-H), 7.75-7.48 (d, *J* = 12.5 Hz, 1H, Ar-H), 7.46-7.34 (d, *J* = 7.5 Hz, 1H, Ar-H), 7.32-7.14 (m, 9H,Ar-H), 6.65 (s, 1H, Ar-H), 2.36 (s, 3H, $COCH_3$), 2.16 (s, 3H, CH_3) (Fig 5 .2); ^{13}C- NMR ($CDCl_3$) δ: 159.64, 143.59, 139.21, 132.46, 129.62, 129.28, 127.87, 121.32,114.32,112.39, 62.49, 55.18, 52.11, 46.07.MS: *m/z* = Cal. 429.44; Found 430.0 (M+1); **Elemental analysis:** Calculated for: $C_{25}H_{20}N_3O_3F$; Calculated: C,69.92 %; H, 4.69%; N, 9.78%; Observed: C, 69.90%; H, 4.66%; N, 9.76% .
6b	**IR: vmax/cm−1:** 3340 (N-H), 2228 (CN), 1698 (CO), 1342–1140 (CF stretching). **1H-NMR (CDCl3) δ:** 9.32 (s, 1H, NH), 7.88-7.86 (d, J = 8.7 Hz, 1H, Ar-H), 7.85-7.77 (d, J = 1.9 Hz, 1H, Ar-H), 7.78-7.76 (d, J = 8.3 Hz, 1H, Ar-H), 7.75-7.48(d, J = 12.5 Hz, 1H, Ar-H), 7.46-7.34 (d, J = 7.5 Hz, 1H, Ar-H), 7.32-7.14 (m, 9H, Ar-H), 6.65 (s, 1H, Ar-H), 2.36 (s, 3H, COCH3), 2.16 (s, 3H, CH3) (Fig 5.7); 13C- NMR (CDCl3) δ: 143.53, 137.36, 135.69, 132.59, 130.27, 129.27, 129.7, 127.79,127.22, 125.56, 60.20, 52.12, 46.15, 21.48 ; MS: m/z = Cal. 495.44; Found 495.0 (M+1). **Elemental analysis:** Calculated for: C26H20N3O4F3: Calculated: C, 63.03 %; H, 4.07%; N, 8.48%; Observed: C, 63.02%; H, 4.04%; N,8.44%.
6c	**IR: vmax/cm^{-1}:** 3340 (N-H), 2228 (CN), 1698 (CO), 1342–1140 (CF streching) **^{1}H-NMR ($CDCl_3$) δ:** 7.43-7.38 (d, *J* = 8.7 Hz, 2H, Ar-H), 7.29-7.18 (m, 9H, Ar-H), 6.96-6.94 (d, J = 8.3 Hz, 1H, Ar-H), 6.72-6.69 (d, J = 12.5 Hz, 1H, Ar-H), 2.52 (s, 3H, COCH3), 2.17 (s, 3H, CH3) ; 13C-NMR (CDCl3) δ: 143.53, 137.37, 135.65, 132.60, 130.28, 129.73, 129.73, 129.59, 127.80, 127.23, 125.51, 60.30, 52.13, 46.15, 21.48, 19.12 (Fig 5.13); MS: m/z = Cal. 480.34; Found 481.8 (M+1) ;

	Elemental analysis: Calculated for: C25H19N3O3Cl2 ; Calculated: C, 62.51 %; H, 3.99%; N, 8.75%. Observed; C, 62.50%; H, 3.97%; N, 8.74%.
6d	**IR: vmax/cm^{-1}:** 3340 (N-H), 2228 (CN), 1698 (CO), 1342–1140 (CF stretching); **^{1}H-NMR ($CDCl_3$) δ:** 7.43-7.38 (d, *J* = 8.7 Hz, 2H, Ar-H), 7.29-7.18 (m, 9H,Ar-H), 6.96-6.94 (d, J = 8.3 Hz, 1H, Ar-H), 6.72-6.69 (d, J = 12.5 Hz, 1H, Ar-H),2.52 (s, 3H, COCH3), 2.17 (s, 3H, CH3); 13C-NMR (CDCl3) δ: 143.52,137.36, 135.65, 132.59, 130.27, 129.73, 129.59, 127.79, 127.23, 125.50, 60.30, 52.12,46.15, 21.48; MS: *m/z* = Cal. 445.90; Found 446.2 (M+1); **Elemental analysis:** Calculated for:$C_{25}H_{20}N_3O_3Cl$; Calculated: C, 67.34 %; H, 4.52%; N, 9.42%. Observed; C, 67.32%; H, 4.49%; N, 9.39%
6e	**IR: vmax/cm^{-1}:** 3340 (N-H), 2228 (CN), 1698 (CO), 1342–1140 (CF stretching); **^{1}H- NMR ($CDCl_3$) δ:** 8.14 (s, 1H, Ar-H), 8.0 (s, 2H, NH), 7.97 (s, 1H, Ar-H), 7.95-7.93(d, J = 8.0 Hz, 1H, Ar-H), 7.70-7.68 (d, J = 8.0 Hz, 1H, Ar-H), 7.62 (s, 2H, Ar-H),7.37 (m, 1H, Ar-H), 7.33-7.31(d, J = 8.0 Hz, 1H, Ar-H), 7.26-7.24 (d, J = 8.3 Hz, 1H,Ar-H), 6.98 (s, 2H, Ar-H), 6.35 (s, 1H, Ar-H), 2.02 (s, 3H, CH3), 1.71 (s, 3H, CH3); **^{13}C-NMR ($CDCl_3$) δ:** 168.9, 164.7, 159.0, 147.5, 138.6, 138.0, 135.8, 134.5, 131.1,130.8, 129.1, 127.5, 125.6, 125.2, 123.8, 123.7, 122.7, 120.7, 118.4, 111.0, 110.7,24.0, 19.0.
6f	**IR: vmax/cm^{-1}:** 3340 (N-H), 2228 (CN), 1698 (CO), 1342–1140 (CF stretching); **^{1}H- NMR ($CDCl_3$) δ:**9.15 (s, 1H, NH), 8.23-8.21 (d, *J* = 8.0 Hz, 1H, Ar-H), 8.08 (s, 1H,NH), 7.92-7.90 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.79 (s, 1H, Ar-H), 7.35 (s, 1H, Ar-H), 7.34(s, 1H, Ar-H), 7.23 (s, 1H, NH), 7.17-7.15 (m, 4H, Ar-H), 6.35 (s, 1H, Ar-H), 3.83 (s,3H, OCH_3), 2.42 (s, 3H, CH_3), 2.04 (s, 3H, CH_3); **^{13}C-NMR ($CDCl_3$) δ:** 172.5, 168.9,164.0, 158.6, 147.5, 138.6, 137.3, 135.8, 128.5, 127.5, 126.7, 126.5, 125.6, 125.2,122.7, 120.7, 118.4, 111.0, 55.8, 24.0, 19.0.
6g	**IR: vmax/cm^{-1}:** 3340 (N-H), 2228 (CN), 1698 (CO), 1342–1140 (CF stretching); **^{1}H- NMR ($CDCl_3$) δ:**9.15 (s, 1H, NH), 8.23-8.20 (d, *J* = 8.0 Hz, 1H, Ar-H), 8.08 (s, 1H,NH), 7.95-7.93 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.79 (s, 1H, Ar-H), 7.47 (d, *J* = 8.0 Hz, 2H,Ar-H), 7.35 (s, 1H, Ar-H), 7.34 (s,

	1H, Ar-H), 7.23 (s, 1H, NH), 7.17-7.15 (m, 4H,Ar-H), 6.35 (s, 1H, Ar-H), 2.42 (s, 3H, CH_3), 2.04 (s, 3H, CH_3), 1.35 (s, 9H, Ar-H); **^{13}C-NMR ($CDCl_3$) δ:** 172.5, 168.9, 158.6, 154.3, 147.5, 138.8, 137.3, 135.8, 131.1,127.5, 127.1, 126.7, 125.6, 125.1, 122.7, 120.7, 118.4, 111.0, 110.7, 34.2, 31.3, 24.0,19.0.
6h	**IR: vmax/cm^{-1}:** 3340 (N-H), 2228 (CN), 1698 (CO), 1342–1140 (CF stretching); **^{1}H- NMR ($CDCl_3$) δ:**9.15 (s, 1H, NH), 8.23-8.20 (d, *J* = 8.0 Hz, 1H, Ar-H), 8.08 (s, 1H,NH), 7.97-7.95 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.79-7.95 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.67-7.65 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.35 (s, 1H, Ar-H), 7.34 (s, 1H, Ar-H), 7.23 (s, 1H,NH), 7.17 (s, 2H, Ar-H), 6.35 (s, 1H, Ar-H), 2.42 (s, 3H, CH_3), 2.04 (s, 3H, CH_3); **^{13}C-NMR ($CDCl_3$) δ:** 172.5, 168.9, 158.6, 147.5, 138.6, 137.7, 135.8, 132.3, 130.1,128.9, 127.5, 126.7, 125.6, 122.7, 120.7, 118.4, 111.0, 110.7, 24.0, 19.0.

2. Biological Evaluation:

The synthesized compounds have been screened for the following biological and pharmacological properties by adopting standard protocols available in literature.

A. Antibacterial activity
B. Anti – inflammatory activity

A. Antibacterial Activity :

- Material and Methods

Staphylococcus aureus (NCIM-5022), a Gram-positive bacteria and *Escherichia coli* (NCIM-5051), a Gram-negative bacteria strain were used to study the antibacterial potency of all the three series of compounds. Bacterial strains of the study were acquired form Pune CSIR-National Chemical Laboratory (NCL) Antibacterial assay was done using disc diffusion method and standard drug used was Chloramphenicol.

- Experimental Procedure

Agar well diffusion technique [12-14] was used for the study of bacterial broth culture under the sterilized condition, from the working culture, a small amount of culture was taken into 10–15 mL sterile 0.9% NaCl solution (normal saline) and was gently mixed together. About 0.5 mL of inoculums and warm agar medium was added to the sterilized Petri dish and was allowed to solidify for about two hours. After incubation period of 24 hours of bacterial strains, bacterial strains were homogeneously smeared on sterilized nutrient agar medium with the help of sterile L-Shaped glass rod. Five uniform wells of 7 mm diameter were bored with the help of cork borer to accommodate 50 µL of the test solution in each well. Solutions of test compounds were prepared by dissolving them in dimethyl sulfoxide to achieve concentration 2.5, 5.0, 10, 20 and 30 µg/50µL (6a-h) using dimethylsulfoxide (DMSO) a negative control. Minimum Inhibitory Concentration (MIC) values obtained from micro dilution method carried out for all the above different series of concentrations.

Ciprofloxacin (10, 50 and 20 µg 50 μL^{-1}) as positive control a standard drug. The test sample (6a-h) minimum inhibitory concentrations values are 50, 50 and 30 µg 50 μL^{-1} per well for all the series of compounds respectively was observed. Samples, control, and standard were loaded into their respective wells using sterile micropipette tips and were incubated for 36 hours at 37 °C.Once the completion of incubation period, the zone of inhibition diameter for each well was measured in mm. The experiments were carried out in triplicates for the series of compounds and the average values of zone of inhibition are tabulated in below table.

Table 3: Antibacterial activity Minimum Inhibitory Concentration (MIC) values of scheme 4.1 (6a-h) derivatives

(+Presence of growth) (- Absence of growth)

B. strains	Conc. (µ g/50 µ L)	Scheme 4.1 comps (6a-h)
Staphylococcus Citrus	2.5	+
	5	+
	10	+
	20	+
	30	-
Staphylococcus aureus	2.5	+
	5	+
	10	+
	20	+
	30	-
Bacillus cereus	2.5	+
	5	+
	10	+
	20	+
	30	-
Bacillus polymyxa	2.5	+
	5	+
	10	+
	20	+
	30	-

Table 4: Antibacterial activities zone of inhibition of 1,2 dihyroquinoline Benzamide derivatives (Scheme 4.1, 6a-h)

Compound	*S. Aureus*	*S. Citreus*	*B. polymyxa*	*B. cereus*
6a	02	13	12	11
6b	**21**	**21**	**20**	**24**
6c	**24**	**28**	**20**	**22**
6d	04	06	06	08
6e	**23**	**26**	**22**	**21**
6f	08	14	13	11
6g	11	17	22	10
6h	**25**	**25**	**22**	**24**
CIPX	28	27	24	24

B. Anti-inflammatory Activity :

- Material and Methods -

The anti-inflammatory activity was performed on Albino Wistar rats of both sexual categories, they are kept at normal test site environment for about one week. Animals were given free admission window to filtered Ultra Violet purified water and typical pelleted feed was given to animals. Indomethacin was used as standard. Test samples of concentrations 100 mg/kg b w and standard Indomethacin concentration of 10 mg/kg body weight was used to perform the assay. 1% carboxy methyl cellulose (CMC) (vehicle) was used for oral route administration to the test systems.

❖ Experimental Procedure -

Carrageenan induced rat paw edema method [25] was performed on albino wistar rats (test system) weighing between 145-175 g, they were arbitrarily separated into fourteen, fourteen and sixteen groups respectively for testing scheme 4.1 6a-h) series of compounds and for standard. Groups of six test animals in each group was starved overnight before tests were started. Group I animals aided as Carrageenan Inducer as control and was administrated with vehicle, Group II aided standard drug indomethacin (10 mg/kg body weight) through oral course. Group III to XV, XVI and XIV groups were given with appropriate samples of tested series of compounds (6a-h) at concentration 100 mg/kg body weight. After administration of samples, test models were observed 30 minutes for a clinical sign. After the period Carrageenan suspension of 0.1 ml of 1% w/v was inoculated into the sub plantar section of the right back paw of each testing model.

Instantly after inoculation, the paw size was measured using digital Plethysmometer, same procedure was repeated at 30, 60, 120 and 180 minute time intervals to measure paw size and the observations are recorded.

Table 5: Anti-inflammatory activity of 1,2-dihydroquinoline benzamide derivatives (Scheme 4.1, 6a-h)

Treatment (Dose mg/kg. p.o.)	Time in minutes			
	30	**60**	**120**	**180**
Carrageenan (1%, 0.1 ml)	0.22±0.100	0.44±0.04	0.54±0.03	0.48±0.091
6a	0.25±0.073	0.31±0.03	0.37±0.00	0.57±0.04
6b	0.35±0.027	0.56±0.02	0.49±0.03	0.52±0.01
6c	0.42±0.080	0.71±0.07	0.59±0.02	0.53±0.02
6d	0.24±0.058	**0.09±0.07*****	**0.06±0.05*****	**0.04±0.03*****
6e	0.09±0.027	0.25±0.01	0.33±0.04	0.40±0.04
6f	0.09±0.027	0.25±0.01	0.33±0.02	0.70±0.04
6g	0.32±0.100	0.34±0.04	0.74±0.03	0.88±0.091
6h	0.24±0.073	0.31±0.03	0.51±0.00	0.67±0.04
Indomethacin (10 mg/kg p.o)	0.27 ± 0.03	0.20 ± 0.06***	0.23 ± 0.06***	0.29 ± 0.06**

Results are presented as mean ± SEM **P <0.01, ***P < 0.001 as compared with standard.

❖ RESULT AND DISCUSSION:

1. Experimental Method:

A series of novel benzamide dihydroquinoline derivatives were synthesized by acetylation of 3-amino phenol, cyclisation of N-(3-hydroxyphenyl) acetamide followed by substitution of o-phenylenediamine to get N-[1-(2- aminophenyl)-4-methyl-2-oxo-1,2-dihydroquinolin-7-yl]acetamide [3]. Compound [3] was treated with various substituted aromatic benzoyl chlorides in order to get the dihydroquinoline derivatives with benzamide moiety [6a-h]. All the derivatives were obtained in good yield. The physical data and structure of all the compounds are presented in **Table 1.**

The spectral data obtained by spectroscopic techniques like FT-IR, 1H NMR, 13C NMR and LCMS or Mass spectra are presented in **Table 2.**

2. Biological Evaluation:

A. Antibacterial Activity:

The series of compounds (6a-h) showed good inhibitory action against tested four strains of bacteria. Initially, antibacterial evaluation at dissimilar concentrations of 2.5, 5.0, 10, 20 and 30 µg/50 µL was tried against the bacterial strains. At concentration 30 µg/50µL and above minimum inhibitory concentration (MIC) was observed for third series of compounds presented in **Table 3** Compounds 6b, 6c, 6e and 6h showed significant activity presented in **Table 4.** It is clear from the data that all the synthesized compounds of the three series possess moderate to good antibacterial activity against Staphylococcus aureus, Staphylococcus citreus, Bacillus polymyxa and Bacillus cereus bacterial strains in comparison to standard Ciprofloxacin.

The molecular docking studies were carried out using LeadIT for antibacterial activity. The Molecular Docking results show that the standard ciprofloxacin has

higher docking energy compared with the newly synthesized compounds. All three series of compounds were docked in to the active sites of Dehydrosqualene synthase (PDB ID: 3ACX) protein effectively.

The fitting of the most potent compounds 6b, 6c, 6e and 6h of Scheme 4.1 were observed to active against docked bacterial protein. This In Silico data and biological data obtained are in agreement

B. Anti-inflammatory Activity:

For series of compounds (6a-h), the increase in right hind paw size was observed after administration of carrageenan (1%, 0.1ml), digital Plethysmometer was used to measure paw size at regular time intermissions 0, 30, 60, 120 and 180 minutes and are reported. Test samples 6a-h was administered orally (100 mg kg-1 of body weight) to test models Albino Wistar rats, significantly suppressed the paw edema. Up to 30 minutes, no change was observed for all the tested compounds, but at 60-minute time interval compounds 6d showed good activity. After 120-minute interval compounds 6d showed very good activity compared to rest of the molecules tested. Finally results obtained at 180 minutes showed compounds were comparable to standard drug Indomethacin as reported in **Table 5.** Results exemplified in **Table 5** against carrageenan induced paw edema method proved that few of the newly synthesized compounds from all the three series showed very good to moderate anti-inflammatory activity. The molecular docking studies were carried out using LeadIT for Antiinflammatory activity. The Molecular Docking result shows that all the newly synthesized compounds have higher docking energy compared with the standard indomethacin. All the compounds from three series were docked in to the active site of COX-1 protein effectively. The docking results and experimentally obtained results are in good agreement.

❖ CONCLUSION:

The antibacterial and anti-inflammatory studies were carried out which revealed that few of our synthesized compounds demonstrated potential activity and potent synthesized compounds can be taken for further studies as these compounds may be possibly pharmacologically potent drugs in future.

❖ ACKNOWLEDGMENT:

The authors are thankful to Professor Dr. Govind Nayak and Dr. Parul Mehta, Director and Principal of Lakshmi Narain College of Pharmacy, Bhopal, India for providing research facilities and encouragement.

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