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SYNTHESIS AND PHARMACOLOGICAL ACTIVITY EVALUATION OF OXADIAZOLES CONTAINING SUBSTITUTED DIHYDROPYRIMIDINONE AND CHLOROQUINOLINE MOITIES

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ABSTRACT: In the present paper, synthesis of new series of 1,3,4-oxadiazole derivatives incorporating substituted dihydropyrimidinone and chloroquinoline moieties 4(a-j) has been reported. All the synthesized compounds were characterized by FTIR, ^{1}H NMR and Mass spectroscopy. The compounds were screened for their in vivo anti-inflammatory activity by the carrageenan induced rat paw edema method and in vitro anti-bacterial activity against some gram positive and gram negative strains of bacteria. This pharmacological activity evaluation revealed that among all the compounds screened, compounds **4c, 4e** and **4g** were found to have promising anti-inflammatory activity. Moreover, compounds **4b, 4c, 4d, 4g** and **4j** exhibited promising anti-bacterial activity against the selected pathogenic strains of bacteria.

INTRODUCTION: Inflammation is a complex defensive mechanism of the body to any noxious stimulus; this process may vary from a localized to a generalized response characterized by the accumulation of fluids and leukocytes leading to edema and pain[1]. Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used to treat the sign and symptoms of inflammation. NSAIDs exert their anti-inflammatory effect mainly through inhibition of cyclooxygenases (COXs), the key enzymes involved in the biosynthesis of prostaglandin from arachidonic acid. There are two COX isoforms COX-1 and COX-2 [2, 3]. Constitutive COX-1 is responsible for providing cytoprotection in gastrointestinal (GI) tract whereas inducible COX-2 mediates inflammation.

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However, the chronic use of NSAIDs may elicit marked gastrointestinal (GI) irritation and ulceration due to their unwanted inhibition of the COX-1 enzyme and the desired blockade of the COX-2 enzyme. The recognition of COX-2 as a potential target has influenced the development of drugs that do not cause GI disorders but retain their clinical efficacy as anti-inflammatory agents [4].

1, 3, 4-oxadiazoles are an important class of heterocyclic compounds with broad spectrum of biological activities. Substituted 1, 3, 4-oxadiazoles have revealed antibacterial, antimycobacterial, antifungal, anti-inflammatory, analgesic, anti-convulsant and anticancer properties [5]. Also the dihydropyrimidinones are known to exhibit a wide range of biological activities such as anti-viral, anti-tumor, anti-oxidant, anti-bacterial and anti-inflammatory properties [6, 7].

In addition, dihydropyrimidinones have emerged as potential calcium channel blockers, anticancer, antihypertensive, α-1a–adrenergic antagonists and neuropeptide antagonists [8].

The dihydropyrimidinone scaffold thus have been studied extensively to expand the existing structure activity relationships and to get further insight into molecular interactions at the receptor level.

Besides, the synthesis of quinolines and their derivatives has been of considerable interest because a large number of natural products and drugs contain this heterocyclic moiety [9]. It is well known that quinolines exhibit a wide range of biological activities [10, 11, 12] and are valuable reagents for the synthesis of nano and mesostructures with enhanced electronic and photonic properties.

In search and design of new drugs, the development of new molecular framework through the combination of different pharmacophores in same mold may lead to compounds with interesting biological profiles.

Prompted by these observations, in the present study, the synthesis and anti-inflammatory screening of new 1,3,4- oxadiazole derivatives incorporating substituted dihydropyrimidinone and chloroquinoline moieties as hybrid molecules possessing anti-inflammatory and anti-bacterial activity are intended.

MATERIALS AND METHODS:

Materials: All common reagents and solvents were used as obtained from commercial supplies without further purifications. Melting points of the synthesized compounds were taken by one end open capillary tubes melting point apparatus and are uncorrected. Infra-Red (IR) spectra were recorded on Shimadzu FTIR 8400S spectrophotometer (KBr) and ^{1}H NMR spectra were recorded on Bruker-Avance (400 MHz) spectrophotometer using DMSO-d_6 solvent and tetramethylsilane (TMS) as an internal standard. Chemical shifts were reported in parts per million (ppm).

Mass spectra were recorded on Waters- Micromass Q-Tof micro Mass Spectrometer. Thin layer chromatography (TLC) was performed using Silica gel G obtained from Merck and the spots were visualized under and iodine vapors.

Developing solvents used were petroleum ether and ethyl acetate (7:3).

Method:

(Synthetic strategy - Scheme 1):

Synthesis of ethyl 6-methyl-2-oxo-4-aryl-1, 2, 3, 4-tetrahydropyrimidine-5-carboxylate 1(a-j): The desired compounds were synthesized using the reported method [13].

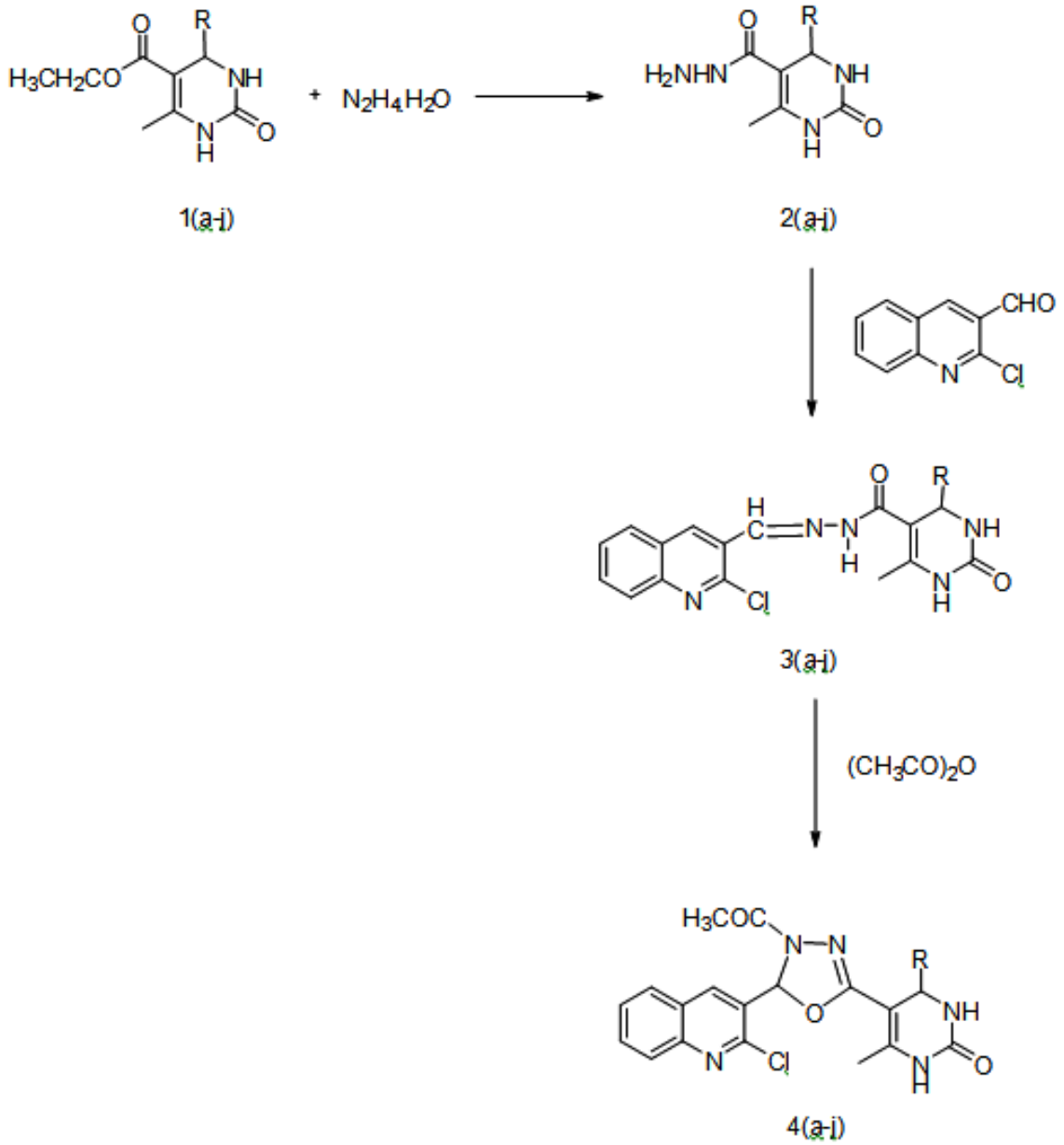
Synthesis of 6-methyl-2-oxo-4-aryl-1, 2, 3, 4-tetrahydropyrimidine-5-carbohydrazide 2(a-j): 0.01 mol of the appropriate dihydropyrimidinones 1(a-j) were dissolved in absolute ethanol and to this 0.01 mol hydrazine hydrate was added. The reaction mixture was refluxed for around 6-7 hr. The completion of reaction was monitored by TLC.

The reaction mixture was allowed to stand overnight and the resulting solid obtained was filtered, dried and crystallized from ethanol.

Synthesis of N'-((2-chloroquinolin-3-yl)methylene)-4-(aryl)-6-methyl-2-oxo-1, 2, 3, 4-tetrahydropyrimidine-5-carbohydrazide 3(a-j): 0.01 mol of the carbohydrazide 2(a-j) in absolute ethanol was warmed with 0.01 mol of 2-chloro quinoline-3-carbaldehyde. The reaction completion was monitored by TLC. The content was poured in ice cold water. The separated product was washed with water, dried and recrystallized from ethanol.

Synthesis of 5-(4-acetyl-5-(2-chloroquinolin-3-yl)-4, 5-dihydro-1, 3, 4-oxadiazol-2-yl)-6-methyl-4-(aryl)-3, 4-dihydropyrimidin-2(1H)-one 4(a-j): 0.01 mol of 3(a-j) was refluxed with 0.01 mol of acetic anhydride at 100°C for 1-2 hrs. The completion of reaction was checked by TLC. The product so obtained was dried and recrystallized from ethanol.

The melting points and corresponding % yields of compounds **4(a-j)** is depicted in **table 1**.



SCHEME 1:

R= C_6H_5, 2-$NO_2C_6H_4$, 3-$NO_2C_6H_4$, 2-OHC_6H_4, 4-OHC_6H_4, 4-$OCH_3C_6H_4$, 4-ClC_6H_4, 4-$N(CH_3)_2C_6H_4$, $C_{10}H_7$, CH=CHPh

TABLE 1: PHYSICAL DATA OF THE SYNTHESIZED COMPOUNDS 4(a-j)

Compounds	R	Mol. formula	Melting point	% yield
4a	C_6H_5	$C_{24}H_{20}ClN_5O_3$	186-188	76
4b	2-$NO_2C_6H_4$	$C_{24}H_{19}ClN_6O_5$	174-176	71
4c	3-$NO_2C_6H_4$	$C_{24}H_{19}ClN_6O_5$	179-180	78
4d	2-OHC_6H_4	$C_{24}H_{20}ClN_5O_4$	170-171	70
4e	4-OHC_6H_4	$C_{24}H_{20}ClN_5O_4$	177-178	79
4f	4-$OCH_3C_6H_4$	$C_{25}H_{22}ClN_5O_4$	182-184	72
4g	4-ClC_6H_4	$C_{24}H_{19}Cl_2N_5O_3$	177-179	71
4h	4-$N(CH_3)_2C_6H_4$	$C_{26}H_{25}ClN_6O_3$	175-177	75
4i	$C_{10}H_7$	$C_{28}H_{22}ClN_5O_3$	181-183	69
4j	CH=CHPh	$C_{26}H_{22}ClN_5O_3$	173-175	77

The Spectral Data of the corresponding compounds is as follows:

Analysis of 5-(4-acetyl-5-(2-chloroquinolin-3-yl)-4,5-dihydro-1,3,4-oxadiazol-2-yl)-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (4a):

IR (KBr, cm^{-1}): 1624 (C=N), 1242(C-O), 1644 (C-C), 3081 (Ar C-H), 1551(C-N), 1706 (C=O), 2952 (C-H). ^{1}H NMR (400 MHz, DMSO-d_6,δ ppm): 9.2 (s, 1H, NH), 7.1-8.3 (m, 10H, Ar-H), 6.8 (s, 1H, CH), 5.2 (s, 1H, CH), 2.3 (s, 3H, CH_3), 2.1 (s, 3H, $COCH_3$). MS: *m/z* 461.13 (M^+, 100%). Anal.Calcd. ($C_{24}H_{20}ClN_5O_3$): C, 62.41; H, 4.36; Cl, 7.68; N, 15.16; O, 10.39. Found: C, 62.18; H, 4.32; Cl, 7.65; N, 15.11; O, 10.37.

Analysis of 5-(4-acetyl-5-(2-chloroquinolin-3-yl)-4,5-dihydro-1,3,4-oxadiazol-2-yl)-6-methyl-4-(2-nitrophenyl)-3,4-dihydropyrimidin-2(1H)-one (4b):

IR (KBr, cm^{-1}): 1631 (C=N), 1236 (C-O), 1649 (C-C), 3089 (Ar C-H), 1549 (C-N), 1702 (C=O), 2958 (C-H). ^{1}H NMR (400 MHz, DMSO-d_6,δ ppm): 9.1 (s, 1H, NH), 7.4-8.4 (m, 9H, Ar-H), 6.7 (s, 1H, CH), 5.2 (s, 1H, CH), 2.4 (s, 3H, CH_3), 2.2 (s, 3H, $COCH_3$).MS: *m/z* 506.11 (M^+, 100%). Anal.Calcd. ($C_{24}H_{19}ClN_6O_5$): C, 56.87; H, 3.78; Cl, 6.99; N, 16.58; O, 15.78. Found: C, 56.82; H, 3.71; Cl, 6.93; N, 16.52; O, 15.74.

Analysis of 5-(4-acetyl-5-(2-chloroquinolin-3-yl)-4,5-dihydro-1,3,4-oxadiazol-2-yl)-6-methyl-4-(3-nitrophenyl)-3,4-dihydropyrimidin-2(1H)-one (4c):

IR (KBr, cm^{-1}): 1629 (C=N), 1231 (C-O), 1651 (C-C), 3087 (Ar C-H), 1549 (C-N), 1705 (C=O), 2961 (C-H). ^{1}H NMR (400 MHz, DMSO-d_6,δ ppm): 9.1 (s, 1H, NH), 7.3-8.5 (m, 9H, Ar-H), 6.5 (s, 1H, CH), 5.1 (s, 1H, CH), 2.4 (s, 3H, CH_3), 2.2 (s, 3H, $COCH_3$). MS: *m/z* 506.11 (M^+, 100%). Anal.Calcd. ($C_{24}H_{19}ClN_6O_5$): C, 56.87; H, 3.78; Cl, 6.99; N, 16.58; O, 15.78. Found: C, 56.81; H, 3.74; Cl, 6.96; N, 16.53; O, 15.76.

Analysis of 5-(4-acetyl-5-(2-chloroquinolin-3-yl)-4,5-dihydro-1,3,4-oxadiazol-2-yl)-4-(2-hydroxy phenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one (4d):

IR (KBr, cm^{-1}): 1630 (C=N), 1233 (C-O), 1644 (C-C), 3082 (Ar C-H), 1547 (C-N), 1695 (C=O), 2947 (C-H). ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 9.8 (s, 1H, OH), 9.0 (s, 1H, NH), 6.7-8.4 (m, 9H, Ar-H), 6.6 (s, 1H, CH), 5.2 (s, 1H, CH), 2.3 (s, 3H, CH_3), 2.1 (s, 3H, $COCH_3$). MS: *m/z* 477.12 (M^+, 100%). Anal.Calcd. ($C_{24}H_{20}ClN_5O_4$): C, 60.32; H, 4.22; Cl, 7.42; N, 14.65; O, 13.39. Found: C, 60.27; H, 4.18; Cl, 7.35; N, 14.62; O, 13.36.

Analysis of 5-(4-acetyl-5-(2-chloroquinolin-3-yl)-4,5-dihydro-1,3,4-oxadiazol-2-yl)-4-(4-hydroxy phenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one (4e):

IR (KBr, cm^{-1}): 1621 (C=N), 1225 (C-O), 1640 (C-C), 3088 (Ar C-H), 1554 (C-N), 1709 (C=O), 2960(C-H). ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 9.6 (s, 1H, OH), 9.2 (s, 1H, NH), 6.9-8.2 (m, 9H, Ar-H), 6.6 (s, 1H, CH), 5.3 (s, 1H, CH), 2.3 (s, 3H, CH_3), 2.0 (s, 3H, $COCH_3$). MS: *m/z* 477.12 (M^+, 100%). Anal.Calcd. ($C_{24}H_{20}ClN_5O_4$): C, 60.32; H, 4.22; Cl, 7.42; N, 14.65; O, 13.39. Found: C, 60.28; H, 4.19; Cl, 7.39; N, 14.63; O, 13.37.

Analysis of 5-(4-acetyl-5-(2-chloroquinolin-3-yl)-4,5-dihydro-1,3,4-oxadiazol-2-yl)-4-(4-methoxy phenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one (4f):

IR (KBr, cm^{-1}): 1633 (C=N), 1242 (C-O), 1645 (C-C), 3082 (Ar C-H), 1543 (C-N), 1701 (C=O), 2947 (C-H). ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 9.1 (s, 1H, NH), 7.1-8.3 (m, 9H, Ar-H), 6.6 (s, 1H, CH), 5.0 (s, 1H, CH), 4.1 (s, 3H, OCH_3), 2.4 (s, 3H, CH_3), 2.1 (s, 3H, $COCH_3$). MS: *m/z* 491.14 (M^+, 100%). Anal.Calcd. ($C_{25}H_{22}ClN_5O_4$): C, 61.04; H, 4.51; Cl, 7.21; N, 14.24; O, 13.01. Found: C, 61.01; H, 4.48; Cl, 7.16; N, 14.20; O, 13.00.

Analysis of 5-(4-acetyl-5-(2-chloroquinolin-3-yl)-4,5-dihydro-1,3,4-oxadiazol-2-yl)-4-(4-chlorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one (4g):

IR (KBr, cm^{-1}): 1628 (C=N), 1230 (C-O), 1647 (C-C), 3085 (Ar C-H), 1547 (C-N), 1703 (C=O), 2961(C-H). ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 9.1 (s, 1H, NH), 7.2-8.4 (m, 9H, Ar-H), 6.7

(s, 1H, CH), 5.2 (s, 1H, CH), 2.3 (s, 3H, CH_3), 2.1 (s, 3H, $COCH_3$). MS: *m/z* 495.09 (M^+, 100%). Anal.Calcd. ($C_{24}H_{19}Cl_2N_5O_3$): C, 58.08; H, 3.86; Cl, 14.29; N, 14.11; O, 9.67. Found: C, 58.04; H, 3.83; Cl, 14.26; N, 14.09; O, 9.64.

Analysis of 5-(4-acetyl-5-(2-chloroquinolin-3-yl)-4,5-dihydro-1,3,4-oxadiazol-2-yl)-4-(4-(dimethylamino)phenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one (4h):

IR (KBr, cm^{-1}): 1623 (C=N), 1237 (C-O), 1645 (C-C), 3081 (Ar C-H), 1544 (C-N), 1698 (C=O), 2956(C-H). ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 9.2 (s, 1H, NH), 6.5-8.1 (m, 9H, Ar-H), 6.3 (s, 1H, CH), 5.0 (s, 1H, CH), 3.1 (s, 3H, NCH_3), 2.4 (s, 3H, CH_3), 2.0 (s, 3H, $COCH_3$). MS: *m/z* 504.17 (M^+, 100%). Anal.Calcd. ($C_{26}H_{25}ClN_6O_3$): C, 61.84; H, 4.99; Cl, 7.02; N, 16.64; O, 9.51. Found: C, 61.81; H, 4.95; Cl, 7.0; N, 16.61; O, 9.48.

Analysis of 5-(4-acetyl-5-(2-chloroquinolin-3-yl)-4,5-dihydro-1,3,4-oxadiazol-2-yl)-6-methyl-4-(naphthalen-1-yl)-3,4-dihydropyrimidin-2(1H)-one (4i):

IR (KBr, cm^{-1}): 1638 (C=N), 1241 (C-O), 1652 (C-C), 3093 (Ar C-H), 1551 (C-N), 1699 (C=O), 2961 (C-H). ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 9.1 (s, 1H, NH), 6.9-8.3 (m, 12H, Ar-H), 6.4 (s, 1H, CH), 5.1(s, 1H, CH), 2.3 (s, 3H, CH_3), 2.0 (s, 3H, $COCH_3$). MS: *m/z* 511.14 (M^+, 100%). Anal.Calcd. ($C_{28}H_{22}ClN_5O_3$): C, 65.69; H, 4.33; Cl, 6.92; N, 13.68; O, 9.38. Found: C, 65.67; H, 4.30; Cl, 6.89; N, 13.66; O, 9.35.

Analysis of 5-(4-acetyl-5-(2-chloroquinolin-3-yl)-4,5-dihydro-1,3,4-oxadiazol-2-yl)-6-methyl-4-styryl-3,4-dihydropyrimidin-2(1H)-one (4j):

IR (KBr, cm^{-1}): 1632 (C=N), 1233 (C-O), 1646 (C-C), 3091 (Ar C-H), 1547 (C-N), 1707 (C=O), 2964 (C-H). ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 8.9 (s, 1H, NH), 7.3-8.3 (m, 10H, Ar-H), 6.5 (s, 1H, CH), 5.9 (s, 1H, NH), 4.8(s, 1H, CH), 2.2 (s, 3H, CH_3), 2.1 (s, 3H, $COCH_3$). MS: *m/z* 487.14 (M^+, 100%). Anal.Calcd. ($C_{26}H_{22}ClN_5O_3$): C, 64.00; H, 4.54; Cl, 7.27; N, 14.35; O, 9.84. Found: C, 63.96; H, 4.51; Cl, 7.23; N, 14.34; O, 9.83.

PHARMACOLOGICAL ASSESMENT:

Anti-inflammatory activity: The *in-vivo* anti-inflammatory activity was assessed by the carrageenan induced hind paw edema method [14]. Wistar rats (either sex) weighing 150-200 g were used for the present study. The experimental protocol for anti-inflammatory activity was approved by the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Ministry of Social Justice and Empowerment, Government of India **(SPCP/ 2013/595-2).**

The animal experiments were performed in accordance with the guidelines for the care and use of laboratory animals; laid down by the CPCSEA. The rats were divided into 12 groups of 6 animals each.

Group I, which served as the control, was given only 0.5% w/v carboxymethyl cellulose (CMC) whereas Diclofenac (10mg/kg) and the synthesized test compounds (50 mg/ kg) were administered orally to the rats of Group II (standard) and the other groups respectively.

After 1hr, all the rats were injected with 0.1 ml of 1% carrageenan solution (freshly prepared in normal saline) in the subplantar aponeurosis of left hind paw to induce inflammation and the volume of injected paw was measured using plethysmometer immediately (at 0 hr). The paw volume was again measured at an interval of 1hr up to 4hr **(table 2).** The average paw volume in a group of treated rats was compared with control group and the percentage inhibition of edema was calculated by using the formula:

$$\text{Percent inhibition} = (1-Vt/Vc) \times 100$$

Where; Vt is the mean paw volume of the test and drug treated rats and Vc is the mean paw volume of the control.

The results obtained are expressed as mean ± S.E.M. (standard error of mean) of six rats. Statistical differences of control and test groups were carried out using the Analysis of Variance (ANOVA) followed by Dunnett's test**.** The difference in results was considered significant when $P < 0.05$

TABLE 2: PERCENT INHIBITION OF CARRAGEENAN INDUCED INFLAMMATION PRODUCED BY COMPOUNDS 4(a-j)

Compounds	Paw volume (ml) ± SEM					% inhibition after 4hr
	0hr	1hr	2hr	3hr	4hr	
Control	0.35±0.009	0.84±0.009	0.91±0.006	0.99±0.008	1.04±0.006	-
Diclofenac	0.34±0.011	0.27±0.009	0.21±0.006	0.15±0.010	0.13±0.008	87.5
4a	0.32±0.009	0.66±0.006	0.59±0.006	0.53±0.006	0.45±0.012*	56.7
4b	0.29±0.006	0.61±0.009	0.55±0.008	0.51±0.009	0.43±0.006	58.6
4c	0.31±0.009	0.62±0.008	0.51±0.006	0.40±0.006	0.29±0.009*	72.1
4d	0.31±0.013	0.70±0.009	0.63±0.012	0.57±0.012	0.52±0.006	50.0
4e	0.32±0.006	0.63±0.006	0.52±0.009	0.44±0.006	0.32±0.013*	69.2
4f	0.28±0.006	0.62±0.009	0.55±0.006	0.50±0.006	0.39±0.009	62.5
4g	0.30±0.012	0.59±0.012	0.45±0.009	0.31±0.013	0.24±0.011	76.9
4h	0.31±0.006	0.74±0.009	0.64±0.013	0.59±0.006	0.55±0.006*	47.1
4i	0.30±0.009	0.69±0.006	0.61±0.006	0.56±0.009	0.49±0.006*	52.8
4j	0.33±0.009	0.71±0.013	0.57±0.006	0.46±0.009	0.36±0.009*	65.4

Data were given in mean ± SEM and analyzed by ANOVA followed by Dunnett's multiple comparison test, (n= 6). ∗ $P < 0.05$ compared to standard drug.

Anti-bacterial activity: The *in-vitro* anti-bacterial activity of the compounds **4(a-j)** was evaluated by the well diffusion method using Hi-Media agar medium against some gram positive (*S. aureus, B. subtilis)* and gram negative *(E. coli, K .pneumoniae)* strains of bacteria. Nutrient broth, subculture, base layer medium and agar medium were prepared according to the standard procedure. Wells were scooped out of agar medium contained in the petri dish which was previously inoculated with the microorganisms. Each test compound (5 mg) was dissolved in ethanol (5 ml, 1000 µg/ml), which was used as sample solution. Sample size for all the compounds was fixed at 0.1 ml. The test compound solution (0.1 ml) was added in the wells and the petri dishes were subsequently incubated at 37°C for 24 h. Ampicillin and Streptomycin were used as reference drugs and ethanol as a negative control. The zones of inhibition thus produced by each compound were measured and compared with the control and the subsequent results are depicted in **table 3.**

The screening results indicate that the compounds **4(a-j)** showed appreciable antibacterial activities against the selected pathogens.

TABLE 3: ANTIBACTERIAL ACTIVITY OF COMPOUNDS 4(a-j)

Compounds	Gram-positive bacteria		Gram-negative bacteria	
	S. aureus	*B. subtilis*	*E. coli*	*K. pneumoniae*
4a	+	+	++	++
4b	+++	++	+++	++
4c	+++	+++	+++	++
4d	++	++	+++	+
4e	+	+	+	-
4f	+	++	+	++
4g	++	+++	+++	++
4h	+	-	-	+
4i	+	+	-	+
4j	++	++	++	++
Ampicillin	+++	++	+++	++
Streptomycin	+++	+++	+++	+++

Key to symbols: inactive = - (inhibition zone < 5 mm); slightly active = + (inhibition zone 5-10 mm); moderately active = + + (inhibition zone 10-15 mm); highly active = + + + (inhibition zone > 15 mm).

RESULTS AND DISCUSSION: The target compounds 5-(4-acetyl-5-(2-chloroquinolin-3-yl)-4,5-dihydro-1,3,4-oxadiazol-2-yl)-6-methyl-4-(aryl)-3,4-dihydropyrimidin-2(1H)-one **4(a-j)** were synthesized using the synthetic strategy outlined in **Scheme 1**.

Reaction progress was duly monitored by TLC. The structures of various synthesized compounds were assigned on the basis of spectral studies. The melting points and corresponding % yields (physical data) of compounds **4(a-j)** is represented in table 1.

The IR, ^{1}H NMR, ^{13}C NMR and Mass spectral data for all the synthesized compounds are represented in experimental protocols.

The IR spectrum of compounds **4(a-j)** reveals a characteristic aromatic stretching within 3093-3081 cm^{-1} .The spectra also showed absorption peak within 1638-1621 cm^{-1} due to C=N stretching vibrations. Spectra also cleared the information regarding the frequency ranging from 1242-1225 cm^{-1} which accounts for the presence of (C-O). The ^{1}H NMR spectra were recorded in DMSO-d_6 using TMS as internal standard. The NMR data of all compounds exhibit multiplet peak between 7.3-8.5 ppm owing to the presence of aromatic protons.

Sharp singlet within 2.0-2.4 ppm range is a characteristic of the methyl protons of the acetyl group. The other signals and peaks of ^{1}H NMR and IR are in complete agreement with the assigned structures. The mass spectra of the requisite compounds displayed a molecular ion peak at appropriate m/z values, which corresponded well with the respective molecular formula. The compounds gave satisfactory results for their elemental analysis.

The synthesized compounds were screened for their in vivo anti-inflammatory activity by the carrageenan induced rat paw edema method. The compounds were tested at dose level of 50 mg/ kg. Observed results reveal that, all the compounds show significant anti-inflammatory activity against control at the said concentration after 4 hours. The percentage inhibition was subsequently calculated after 4 hr.

The compounds exhibited anti-inflammatory activity ranging from 47.1% to 76.9% (table 2), when compared to standard drug Diclofenac (87.5%). Compounds **4c** and **4g** were found to be potent anti-inflammatory agents while **4e, 4f** and **4j** were found to be moderately active agents.

Besides, in vitro anti-bacterial activity for the synthesized compounds was also evaluated against some gram positive and gram negative strains of bacteria using the well diffusion method. Compounds **4b, 4c, 4d** and **4g** were found to be highly active against all the tested strains of bacteria showing the broadest spectrum of antibacterial activity while **4a, 4e, 4f** and **4j** were found to be moderately active against the selected pathogens. Thus, the combined observed results of the *in-vivo and in-vitro* studies infer that the synthesized compounds may be utilized as potent anti-inflammatory and anti-bacterial agents.

CONCLUSION: A series of 1, 3, 4- oxadiazole derivatives incorporating substituted dihydro-pyrimidinone and chloroquinoline moieties were synthesized in good yield. The compounds were evaluated for their *in vivo* anti-inflammatory activity by the carrageenan induced rat paw edema method and *in vitro* anti-bacterial activity against some selected pathogenic strains of bacteria.

Compounds **4c** and **4g** were found to be potent anti-inflammatory agents with a percent inhibition after 4hr of 72.1 and 76.9 respectively in comparison to standard reference drug (Diclofenac) at a dose of 50 mg/ kg. Compounds **4b, 4c, 4d, 4g** and **4j** were found to be the most active antibacterial agents among the synthesized derivatives when compared to reference drug Ampicillin and Streptomycin at a dose of 1000 µg/ml.

The present study revealed that the synthesized compounds can be used as anti-inflammatory and anti-bacterial agents with great potential.

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