Review on synthesis and screening of the quinoline derivatives as an anti-inflammatory agent

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Abstract—**Inflammation, a natural defense mechanism, plays a crucial role in protecting living tissues from injury, toxins, and infection. However, excessive release of cytokines can lead to chronic inflammation, contributing to diseases such as cancer and depression. Quinoline derivatives have shown significant promise in medicinal chemistry, possessing analgesic, anti-inflammatory, and anti-cancer properties. This study explores the synthesis and pharmacological activities of quinoline-based compounds, including 7-aminoquinoline derivatives and triazolo-quinolones. The synthesized compounds were characterized using various spectroscopic techniques and evaluated for their anti-inflammatory activity, showing significant edema reduction in mice and rats. The results demonstrate the potential of quinoline derivatives as safer anti-inflammatory agents, with compounds 1A and 1E exhibiting stronger anti-inflammatory action. However, potential side effects, such as gastrointestinal issues and liver enzyme elevation, were also noted. This research contributes to the development of novel quinoline-based anti-inflammatory agents, offering a promising alternative to traditional nsaids.**

I. INTRODUCTION

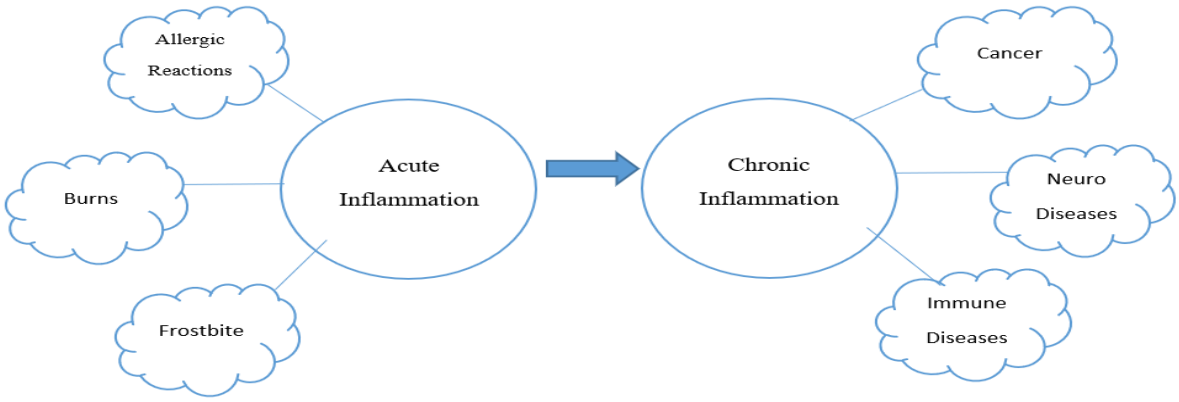
A localised metabolic reaction of living tissue is called inflammation. The word comes from the Latin "inflammare," which meaning burn. Similar to inflammation, tissue damage, and toxins, inflammation may be a complex defence response that is brought on by a variety of circumstances. [1] The unconscious process initiates general tissue regeneration and helps to eradicate harmful impulses. [2] Excessive cytokine release and concurrent inflammatory cell migration to the afflicted areas may lead to chronic inflammation and infection. [3] Pro-inflammatory mediators such as neoplasm mortification factor-alpha (TNF-α), interleukin-1beta (IL-1β), and IL-6 are released by fibroblasts in response to inflammatory stimulation. They also maintain autacoid synthesis, which leads to more inflammatory reactions. [4]

Immune system stimulation cells will produce more pro-inflammatory proteins and enzymes, such as inducible gas synthase (inos) and Cox-2 (COX 2), which cause the release of autacoid and nitric oxide (NO), respectively. Later on, NO and COX cause inflammatory reactions that are linked to the development of degenerative diseases including cancer and depression. [5] Quinoline moiety derivatives are essential for the creation of new drug classes with a range of biological properties, such as analgesia, anti-inflammatory, anti-tubercular, anti-bacterial, anti-cancer, and anti-malarial [6–9]. [10–13] Non-steroidal anti-inflammatory medications (nsaids) and analgesics include glafenine, floctafenine, and antrafenine. Medication that falls within this category and could be considered 4-aminoquinolines. [14, 15]

The pharmacophoric moiety indicates that the action is caused by the addition of another heteroatom moiety to the quinolone ring. [16] The 7-chloro-4-(piperazin1-yl)quinolone in the meantime. The antimalarial medication piperaquine's basic structure serves as its skeleton, supporting this ingredient as an effective addition to many medications. [17] Analgesics and non-steroidal anti-inflammatory medicines are recommended to alleviate pain and improve the patient's quality of life. [18] Studies are still necessary for safer candidates, despite the fact that they are usually connected with goods. The synthesis and tube-shaped structure of epithelial growth problem receptor II are shown.

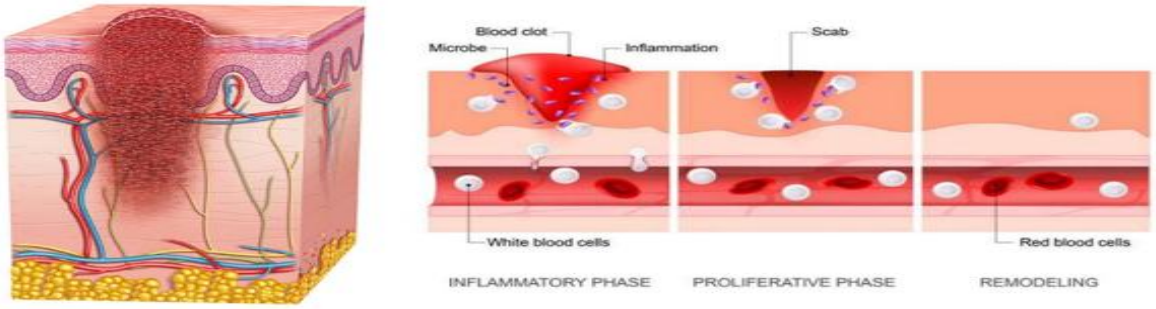
Inflammatory types: Inflammation comes in two flavours: acute and chronic.

1. Acute Inflammation.
2. Chronic Inflammation.



Stages of the Inflammation :

1. Inflammatory Stage.
2. Proliferative Stage.
3. Remodeling Stage.



Numerous cancer forms are linked to chronic inflammation, and the majority of solid tumours have inflammatory indications. Tumour initiation, development, and progression are significantly influenced by immune cells. Pro inflammatory cytokines such as interleukin-6 (IL-6) and tumour necrosis factor (TNF)-α control several of these effects. TNF-α and IL-6 are interesting candidates for adjuvant treatment in cancer because they are master regulators of tumor-related inflammation and carcinogenesis[19]. Depending on the kind of structure, quinolone analogues display a variety of biological actions in the therapeutic setting[20]. In addition to being significant substances, 2,4-dihydroxyquinolines have a number of intriguing pharmacological characteristics. Alkaloids with pyrano [3,2-c] Pyrano and pyridone [3,2-c] Quinolone moieties exhibit a wide range of biological actions. Fusaricide, melicobisquinolinone-B, zanthosi muline, and huajiaosimuline are just a few of these alkaloids are considered to as possible anticancer medicines since they show cytotoxicity against cancer cells. [21,22]nsaids, or non-steroidal anti-inflammatory medications, are used useful instruments for treating fever, discomfort, and both acute and chronic inflammation. But long-term clinical use nsaids is linked to serious adverse effects include bleeding, nephrotoxicity, and gastrointestinal ulcers.Thus, finding novel and safer anti-inflammatory medications is a difficult objective for this field of study [23].

The development of substances with a safer anti-inflammatory profile is constantly needed. In recent years, there has been a lot of interest in the synthesis of different heteroannulated quinoline derivatives [24]. These compounds are the structural frameworks of several naturally occurring compounds that exhibit a wide range of biological activities, including antituberular [25], antibacterial [26,27]], anti-inflammatory [28], antioxidant [29], antimalarial, diuretic, clastogenic, antimicrobial [30,31], antitubulin [32], and as antiprion agents [33]. Since the quinoline moiety contains analgesic and

anti-inflammatory properties [34], it has been observed that adding more heterocyclic rings to the quinoline core tends to have a significant impact on boosting the activity [35,].

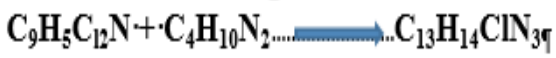
II. MATERIALS

1. Piperazine.
2. Potassium Carbonate.
3. Isopropyl alcohol Dichloromethane.
4. Ammonia Pyridine.
5. Dichloromethane.
6. Ammonia Pyridine.
7. Aniline.
8. Phenyl hydrazine.
9. 4-aminobenzoic acid.
10. Acetic acid.
11. Phosphorus oxychloride.

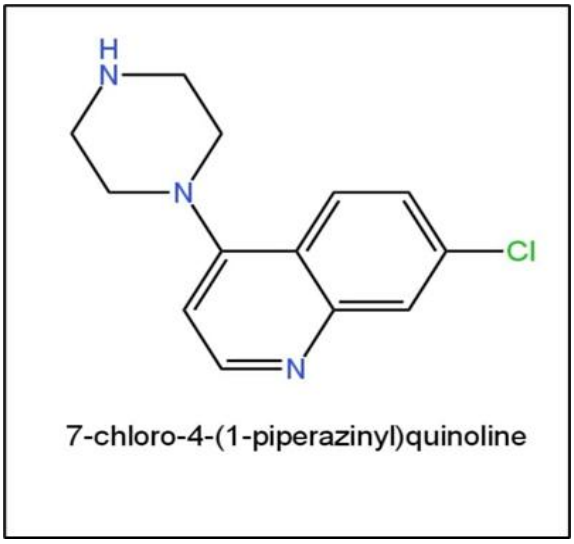
III. METHODOLOGY

1. Make plans to prepare the derivatives of 7-amino quinoline (1A-1E). Regarding 1-yl) quinoline (7-chloro-4 (Piperazine) (1A)

To combine 6.4 grams of anhydrous piperazine, 3.45 grams of potassium carbonate, and 4.9 grams of 4,7 dichloroquinoline in 35 milliliters of isopropyl alcohol. For eighteen hours, reflux it at 50–60°C. Reduced pressure was used to extract the solvent after allowing it to return to ambient temperature. The reaction mixture was dissolved in 150/150 ml of dichloromethane and water. After separating the organic phase and giving it another water wash, 50% aqueous acetic acid was added to bring the ph down to 4-4.5. Before being extracted using dichloromethane, the aqueous layer was separated and basified by adding liquid ammonia. After removing the solvent with less pressure, the residue was titrated for an hour in hexane. They filtered off the solid[36].



$C_{13}H_{14}ClN_3$



7-chloro-4-(1-piperazinyl)quinoline

The bicyclic quinoline ring system, a fused aromatic ring structure composed of a pyridine and a benzene ring, is the foundation of this structure. At the quinoline's 4-position, a piperazine ring a six-membered ring with two nitrogen atoms is joined, and at its 7-position, a chlorine atom. This substance is a simplified structural analogue of piperaquine, an antimalarial medication.

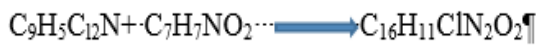
Mechanism of Action:

Inflammatory mediators are suppressed to produce the anti-inflammatory action. Effective derivatives considerably reduced the levels and gene expression of important inflammatory markers, such as nitric oxide (NO), inducible nitric oxide synthase (iNOS), cyclooxygenase-2 (COX-2), tumour necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1beta (IL-1β), in experiments employing macrophage cell cultures and mouse models.

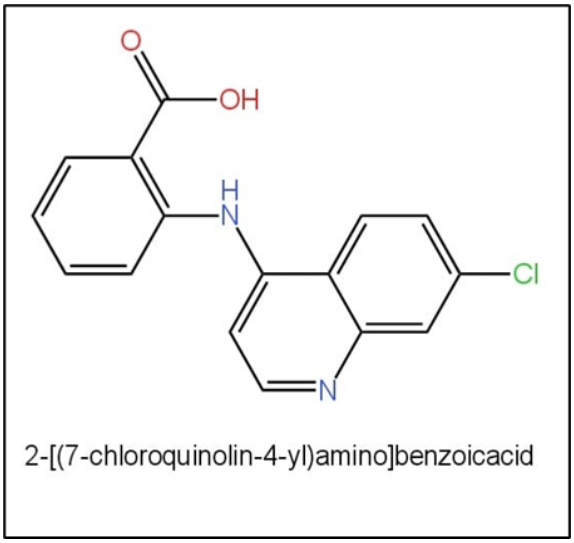
2. Regarding 4-(7-chloroquinolin-4-yl) benzoic acid (1B)

To mix 6.4 grams of anhydrous amino benzoic acid, 3.45 grams of potassium carbonate, and 4.9 grams of 4,7-dichloroquinoline in 35 milliliters of isopropyl alcohol. For 18 hours, reflux it at 50–60°C. Reduced pressure was used to extract the solvent after allowing it to return to ambient temperature. The reaction mixture was dissolved in 150/150 ml of dichloromethane and water. After separating the organic phase and giving it another water wash, 50% aqueous acetic acid was added to bring the ph down to

4-4.5. Before being extracted using dichloromethane, the aqueous layer was separated and basified by adding liquid ammonia. After removing the solvent with less pressure, the residue was titrated for an hour in hexane. They filtered off the solid[36].



$C_{16}H_{11}ClN_2O_2$



Glafenic acid, 3-(4-chloroquinazolin-2-yl)phenyl acetate, and 3-(4-chloroanilino)-1-phenylpyrrole-2,5-dione are among the several chemical compounds that can be represented by the molecular formula $C_{16}H_{11}ClN_2O_2$. Since many alternative chemical structures can have the same formula, the particular substance depends on how the atoms are arranged.

Mechanism of action:
Studies have shown that several compounds containing a pyrazole nucleus, including (5-chloro-2-hydroxyphenyl)-(1-phenylpyrazol-4-yl)methanone, have anti-inflammatory properties. In particular, a number of synthesised pyrazole derivatives demonstrated strong anti-inflammatory action; several of these molecules were more effective than the study's reference medication. The carrageenan-induced rat paw oedema experiment, a common in vivo paradigm for evaluating inflammation, was used to investigate the anti-inflammatory effects. Increased anti-inflammatory effect has been associated with the presence of an acidic group, such as an enolic centre (found in the pyrazolone structure associated with this molecule) or a carboxylic acid. The particular substance in question might belong to a larger class of compounds under investigation for possible therapeutic uses, such as anti-inflammatory ones.

3. Regarding yl-4-phenylquinoline-7-chloro-2-hydrazine (1C)
In 35 milliliters of isopropyl alcohol, combine phenyl hydrazine (7.57 milliliters), potassium carbonate (3.45 grams), and 4,7 dichloroquinoline (4.9 grams). For eighteen hours, reflux it at 50–60°C. Reduced pressure was used to extract the solvent after allowing it to return to ambient temperature. The reaction mixture was dissolved in 150/150 ml of dichloromethane and water. After separating the organic phase and giving it another water wash, 50% aqueous acetic acid was added to bring the ph down to 4-4.5. Before being extracted using dichloromethane, the aqueous layer was separated and basified by adding liquid ammonia. After removing the solvent with less pressure, the residue was titrated for an hour in hexane. They filtered off the solid[36].

- Phenylhydrazine | C6H5NHNH2 | CID 7516 - PubChem - NIH

Phenylhydrazine * C6H8N2 * C6H5NHNH2 ... * 2005-03-26. * 2025-11-15. ... * 1 Structures. 1.1 2D Structure. Structure Search. 1.2 3
National Institutes of Health (NIH) | (.gov)

- 4,7-Dichloroquinoline = 99 86-98-6 - Sigma-Aldrich

About This Item * Empirical Formula (Hill Notation): C9H5Cl2N. * 86-98-6. * Molecular Weight: 198.05. * Beilstein: 125359. * EC Nu...
Sigma-Aldrich

- Phenylhydrazine | C6H5NHNH2 | CID 7516 - PubChem

Phenylhydrazine * C6H8N2 * C6H5NHNH2
National Institutes of Health (NIH) | (.gov)

- 4, 7-Dichloroquinoline is a chemical compound ... - Ankleshwar

The "4, 7-dichloro" prefix indicates that there are chlorine atoms attached to the quinoline ring at positions 4 and 7. This compo...

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- (a) Ultrasonic reaction of 4,7-dichloroquinoline (1) with... | Download Scientific Diagram

nucleophilic substitution reaction 4,7-dichloroquinoline (1) with thiosemicarbazide (2) utilizing ultrasonic irradiation for 3...

ResearchGate

- Degree of unsaturation in the major product of following reacti...

7 Jan 2025 — Step 2 Determine the molecular formula of the product formed after the reaction with KOBr.

Filo

- What product would you expect to obtain from the photochemical ...

3 Nov 2023 — Text Solution Text solution verified icon Verified Step 1. Identify the reactants The reactants are (2E,4Z,6E)-2,4,6-oct...

Filo

- When alkyne A is treated with \operatorname {NaNH}{2} followed b...

31 May 2024 — Step 2. Identify the possible products formed and calculate their molecular formulae.

- Preparation and Antibacterial Activity of Some New 4-(2 ...

14 Jan 2018 — Reactions between the aldehydes 3a–f and 7-chloro-4-hydrazinylquinoline 2, obtained from reaction of 4,7-dichloroquinol...

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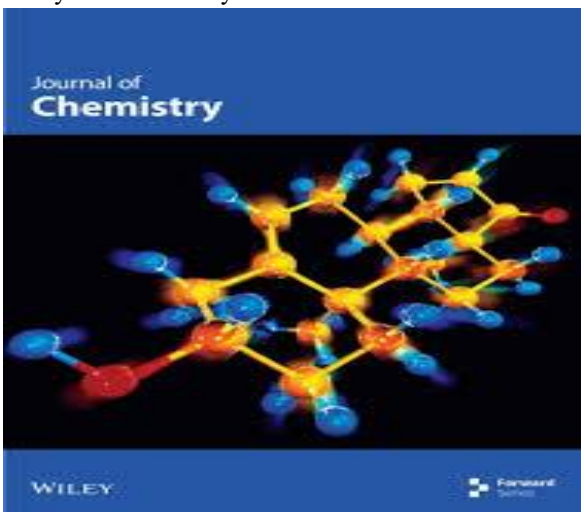
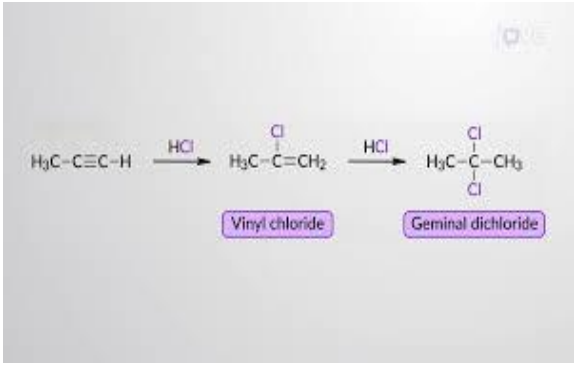


- Video: Electrophilic Addition to Alkynes: Hydrohalogenation

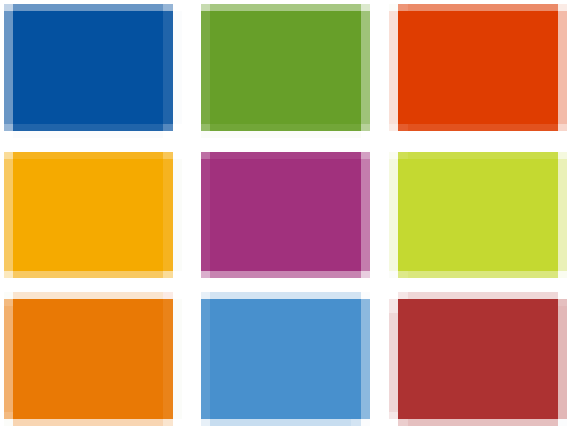
21 May 2025 — The net result is a trans addition of hydrogen from one HCl and a chloride from the other HCl to form a chloroalkene. T...

JoVE



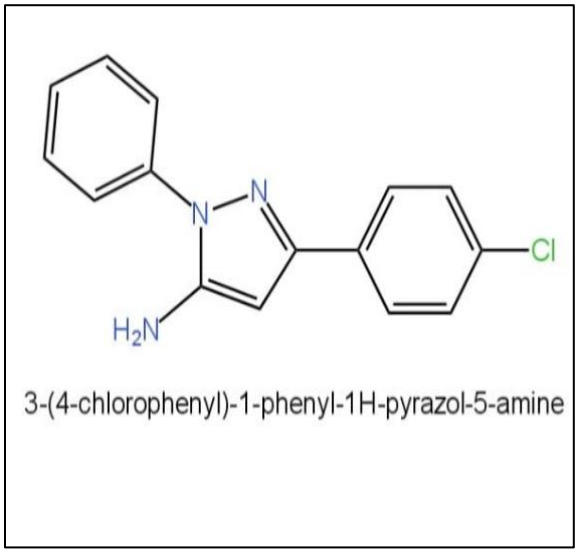
Crystal structure of tris(4,7-diphenyl-1,10-phenanthroline-κ2N,N′)cobalt(III) tris(hexafluoro-phosphate) monohydrate

14 Mar 2022 — The obtained compound was oxidized with chlorine gas made in situ to convert Co II to Co III. Finally, the substitution...



IUCr Journals

$C_{15}H_{12}ClN_3$



3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-5-amine

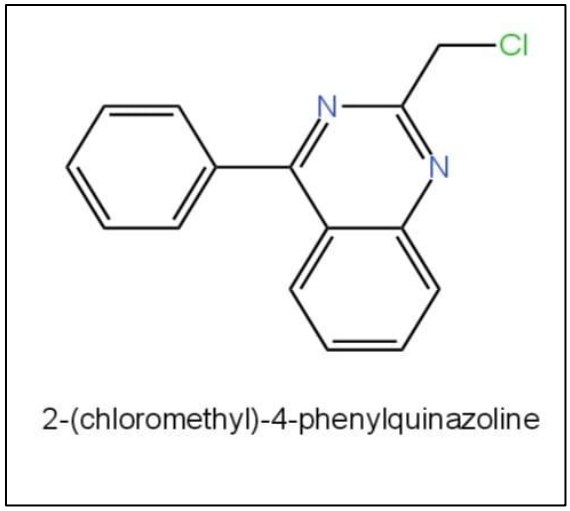
Numerous pyrazole and quinazoline derivatives have been investigated as strong and specific inhibitors of cyclooxygenase-2 (COX-2), a mechanism shared by non-steroidal anti-inflammatory medications (NSAIDs). In animal models, certain pyrazole compounds have shown notable anti-inflammatory benefits, such as lowering paw oedema caused by carrageenan.

4. 4-(7-chloro-1,2-dihydroquinolin-4-yl)aniline (1D) synthesis

Aniline (6.91 ml), potassium carbonate (3.45 gm), and 4,7-dichloroquinoline (4.9 gm) are combined in 35 ml of isopropyl alcohol. For eighteen hours, reflux it at 50–60°C. Reduced pressure was used to extract the solvent after allowing it to return to ambient temperature. The reaction mixture was dissolved in 150/150 ml of dichloromethane and water. After separating the organic phase and giving it another water wash, 50% aqueous acetic acid was added to bring the ph down to 4-4.5. Before being extracted using dichloromethane, the aqueous layer was separated and basified by adding liquid ammonia. After removing the solvent at lower pressure, the residue was titrated for an hour in hexane. They filtered off the solid[36].

$C_9H_5Cl_2N + C_6H_7N \longrightarrow C_{15}H_{11}ClN_2 + HCl$

$C_{15}H_{11}ClN_2$



2-(chloromethyl)-4-phenylquinazoline

Search results confirm that compounds with similar structures (such as quinoline and quinazoline derivatives, and N-acylhydrazone derivatives) exhibit significant anti-inflammatory and analgesic effects in various studies, even though they do not identify a single, specific, well-known anti-inflammatory drug with the exact formula. These related chemicals frequently have the following mechanisms of action: suppression of inflammatory mediators such as nitric oxide (NO), prostaglandins (PGs), and leukotrienes (LTs). Pro-inflammatory cytokines including IL-6, TNF-alpha, IL-17, and IFN-gamma are suppressed. alteration of the activity of certain enzymes, such as inducible nitric oxide synthase (iNOS) and cyclooxygenase (COX). Human red blood cell (HRBC) membrane stabilisation is an in vitro indicator of anti-inflammatory properties.

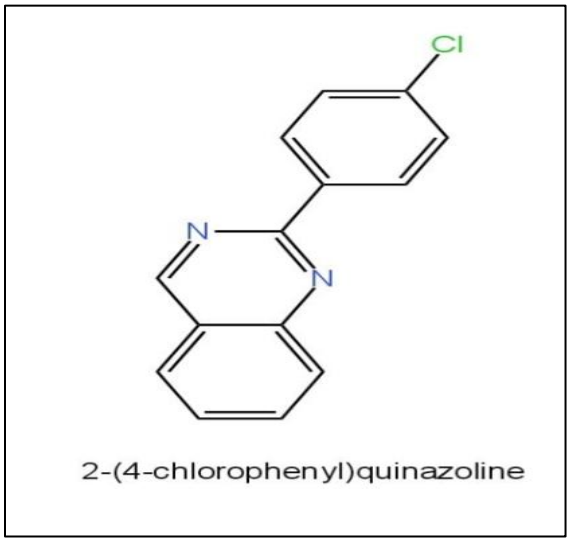
5. 7-chloro-4-(pyridine-1-yl)quinoline synthesis (1E)

Pyridine (6 ml), potassium carbonate (3.45 gm), and 4,7dichloroquinoline (4.9 gm) are combined in 35 ml of isopropyl alcohol. For eighteen hours, reflux it at 50–60°C. Reduced pressure was used to extract the solvent after allowing it to return to ambient temperature. The reaction mixture was dissolved in 150/150 ml of dichloromethane and water. After separating the organic phase and giving it another water wash, 50% aqueous acetic acid was added to bring the ph down to 4-4.5. Before being extracted using dichloromethane, the aqueous layer was separated and basified by adding liquid ammonia. After removing the solvent at lower pressure, the

residue was titrated for an hour in hexane. They filtered off the solid [36].

$$C_9H_5C_{12}N + C_5H_5N \longrightarrow C_{14}H_{10}ClN_2^+ + [Cl^-]$$

$C_{14}H_{10}ClN_2$



Cyclooxygenase (COX) enzyme inhibition: These substances prevent the production of prostaglandins, which are important mediators of fever, pain, and inflammation. Reduction of inflammatory mediators: They can lower nitric oxide (NO) and pro-inflammatory cytokines such TNF-α, IL-6, and IL-1β. Numerous plant-derived substances, including certain flavonoids and triterpenoids with molecular weights similar to the molecule in issue, have strong anti-inflammatory effects via influencing these same pathways, according to research on natural products.

7-Alkoxy-1-amino-4,5-dihydro[1,2,4]triazole[4,3-a]quinolone (anti-inflammatory)

Compounds 2a-2p were produced when the starting material 6-hydroxy-3,4-dihydro-2(1H)-quinolone interacted with a suitable quantity of alkyl halide in a sodium hydroxide solution in 100% methanol or n butanol (for 2o only). Since the strong electron-donor activity of the p-methoxy in the phenyl ring would increase the stability of the positive ion of carbon in the benzyl group and, therefore, decrease the rate of nucleophilic substitution, compound 2o (6-(4-methoxybenzyloxy) quinoline-2-one) was prepared using n-butanol as the solvent rather than ethanol and KI as the catalyst. However, only a moderate yield was obtained for this compound. Compounds 2a–2o were reacted with phosphorous pentasulfide in acetonitrile with triethylamine to create compounds 3a–3o.

Dioxane was used as a sol vent because compound 2p (6-(2,4-dichlorobenzyloxy)quinoline-2-one) did not dissolve in acetonitrile. With stirring and refluxing for 24 hours, compound 2p and phosphorous pentasulfide reacted in dioxane to produce 3p (6-(2,4-dichloro-benzyloxy)-quinoline 2-thione) with a moderate yield. In THF, compounds 3a–3p underwent further reaction with hydrazine hydrate to produce compounds 4a–4p. In short, a solution of compounds 3a and 3p in THF was added dropwise to a solution of hydrazine hydrate in THF at ambient temperature, and the mixture was agitated for one hour at 608C. The product was then crystallized in petroleum ether after half of the solvent was extracted at lower pressure. After filtering and washing with petroleum ether, the precipitate was stored below 80C.

The resulting chemicals were sufficiently pure for the following stage. As seen in Scheme 2, the molecular weight suggested that hydrazine was substituted with compounds 3a–3p, and the structures of compounds 4a–4p may alter gradually over the course of 10 hours at ambient temperature. However, by maintaining compounds 4a–4p below 08C, this shift might be prevented. A suitable volume (about one fifth of the dioxane volume) of aqueous Na2CO3 solution was absolutely required in order to react 4a–4p with cyanogene bromide in dioxane , yielding the target compounds 5a–5p . IR, 1H-NMR, MS, and elemental analysis were used to characterize the produced chemicals[37,38,39,40,41].

Synthesis of 2-chloro-3-formyl quinoline

At 0–5°C, anhydrous dimethyl formamide (DMF) (2.19g, 0.03 mol) was mixed with phosphorus oxychloride (pocl3) (13.77g, 0.09 mol) dropwise for 5 minutes. After adding acetanilide (1.35g, 0.01 mol) to the mixture above, it was refluxed for eight hours at 75–80°C. When the reaction liquid was cooled and then stirred while being placed into crushed ice, a pale yellow precipitate of 2-chloro-3-formyl quinoline formed right away. To get the chemical, the precipitate was filtered, cleaned with water, and recrystallised from ethyl acetate[42,43].

IV. DISCUSSION

Physicochemical properties of synthesized 7- aminoquinoline derivatives (1A 1E) :-

Sr. No.	Sample	Mol. formula	Melting point	% yield	Rf value	Mol. Weight
1.	A	$C_{13}H_{14}CIN_3$	282	58	0.81	247
2.	B	$C_{15}H_9CINCOOH$	275	78	0.71	282
3.	C	$C_{15}H_{12}CIN_3$	276	55	0.73	268
4.	D	$C_{15}H_{13}CIN_2$	300	64	0.61	255
5.	E	$C_{14}H_{11}CIN_2$	286	46	0.81	242

[36]

Pharmacological activity :-

Anti-inflammatory properties

When it comes to anti-inflammatory chemicals, A, E, and others appear to be more active than others.

Anti inflammatory activity

(7-Alkoxy-1-amino-4,5-dihydro[1,2,4]triazole[4,3-a]quinolone (anti-inflammatory)

An in-vivo inhibitory experiment tracking xylene-induced ear edema was used to assess the anti-inflammatory efficacy [19]. All investigated substances were given orally to Kunming mice (20–25 g body weight, 10 animals per group) after being homogenized with 0.5% sodium carboxyme thylcellulose (CMC-Na). Only the vehicle (0.5% sodium carboxy methyl cellulose, 0.2 ml/10 g) was given to the control animals. A micropipette was used to apply 20 ll of xylene to each mouse's right ear surface at a predetermined later time. Thirty minutes after the mice were euthanized, a cylindrical plug (7 mm in diameter) was removed from both the treated and untreated ears. The weight difference between the two plugs was used to measure edema. The percentage of edema decrease in comparison to the control group that received CMC-Na was used to represent the anti-inflammatory activity. Ibuprofen, an NSAID, was examined concurrently as an activity reference. Student's t-test was used to statistically compare edema results, which were represented as mean standard deviation. The significance test was set at a threshold of $p < 0.05$[41].

Anti-Inflammatory Properties(2-chloro,3-formyl quinolone)

Compounds with an azetidinone molecule at position three of the quinoline nucleus have significant anti-inflammatory effect, according to the structural activity connection. The anti-inflammatory activity of compounds 6a–l ranged from 23.37 to 60.32 percent.

Pharmacological Screening for (2-chloro,3-formyl quinolone)

Animals

For the acute toxicity investigation, female Swiss albino mice weighing 25–30 g were employed. For anti-inflammatory efficacy, male albino Wistar rats weighing between 200 and 220 grammes were employed. The institutional animal ethics committee approved the study protocol. Lucknow, India's Hygia Institute of Pharmaceutical Education & Research (1088/2015) CPCSEA). The animals were obtained from the CSIR Indian Institute of Toxicology Research in Lucknow, India, and kept in individual polypropylene cages with 12-hour light-and-dark cycles at a constant temperature of 25 ± 2°C and 35–60% relative humidity. The animals were given free access to water and a typical rat pellet diet[44].

Acute Toxicity

In order to determine the safety profile of the compounds and to determine the effective dose of the test compounds, the acute oral toxicity test was conducted in accordance with OECD 423 guidelines (OECD, 2000). For each chemical, five groups of six female Swiss albino mice weighing 25–30 g were created. Before the test, the animals were famished for 24 hours and given unlimited access to water. Animals were given several chemicals orally at increasing doses of 5, 50, 300, 2000, and 5000 mg/kg b.w. On the day of the experiment[44].

Rat Paw Method Induced by Carrageenan

An in vivo rat hind paw oedema model generated by carrageenan was used to assess the anti-inflammatory properties of the synthesised compounds. A popular animal paradigm for assessing the anti-inflammatory

properties of recently synthesised compounds is the carrageenan-induced rat paw oedema model. In this model, measurements were made to evaluate the test compound's capacity to lessen localised oedema caused in the rat paw by injecting carrageenan, an irritating agent. The animals were split up into groups of fourteen at random. As a control group, Group I was given a solution containing only 0.5% carboxymethyl cellulose (CMC). Group II was the control group and was given diclofenac (20 mg/kg; p.o.). Each rat received a subcutaneous injection of 0.1 ml of carrageenan solution (0.1% in sterile 0.9% nacl solution) into the sub-plantar region of their right hind paw half an hour after the test compounds (20 mg/kg; p.o.) And the standard medication were administered. Saline displacement displayed on the screen at 0, 1, 2, and 4 hours following carrageenan injection was used to measure the paw volume using a digital plethysmometer. The following formula was used to calculate the percentage inhibition of oedema: Anti-inflammatory activity (% inhibition) = 100 (Vc–Vt/Vc). The oedema volumes in the control group (Vc) and the test compound-treated groups (Vt) were assessed.

The control group's paw volume is denoted by Vc, while the test group's paw volume is denoted by Vt[41,44].

Potential Side effects of quinoline derivatives as an anti-inflammatory agents

Gastrointestinal Problems: Some quinoline derivatives might cause diarrhoea or upset stomachs, just like other non-steroidal anti-inflammatory medicines (nsaids).

Abnormalities of Liver Function: Increased liver enzymes found by blood testing can be a negative effect, especially with some nsaids.

Fluid Retention and High Blood Pressure: Some derivatives may lead to salt and fluid retention, which can contribute to elevated blood pressure.

Long-Term Risks: In some instances, animal research has connected quinoline exposure to a possible elevated risk of developing specific cancers.

Other Mechanisms: Some quinoline derivatives can interfere with processes like DNA synthesis, cell division, or the activation of neurotransmitters, which may appear as specific detrimental effects depending on their specific target.

V. CONCLUSION

In conclusion, inflammation is a complex and multifaceted biological response that plays a crucial role in protecting the body against injury, toxins, and infection. However, excessive or chronic inflammation can lead to various diseases, including cancer and depression. The study of quinoline derivatives has shown promising results in the development of anti-inflammatory agents, with compounds such as 7-aminoquinoline derivatives and triazolo-quinolones exhibiting significant anti-inflammatory activity.

The synthesis of these compounds using various nucleophiles and reaction conditions has been successfully demonstrated, and their pharmacological activities have been evaluated using in vivo and in vitro models. The results show that quinoline-based anti-inflammatory agents have the potential to provide safer and more effective alternatives to traditional nsaids, which are often associated with gastrointestinal issues, liver enzyme elevation, and other side effects.

However, further research is needed to fully explore the potential benefits and risks of quinoline-based anti-inflammatory agents, including their potential side effects, such as gastrointestinal issues, liver enzyme elevation, and possible long-term carcinogenic risk. Additionally, the development of new quinoline derivatives with improved pharmacological profiles and reduced side effects is an area of ongoing research.

Overall, the study of quinoline derivatives and their anti-inflammatory activities has contributed significantly to our understanding of the complex mechanisms of inflammation and has the potential to lead to the development of new and innovative treatments for various inflammatory diseases. Future research should focus on optimizing the synthesis and pharmacological activities of quinoline derivatives, as well as exploring their potential therapeutic applications in a clinical setting.

Recommendations For Future Research

1. Optimization of Quinoline Derivative Synthesis: Further research is needed to optimize the synthesis of quinoline derivatives, including the development of more efficient and cost-effective methods.
2. Pharmacological Evaluation: In-depth pharmacological evaluation of quinoline derivatives is

necessary to fully understand their anti-inflammatory activities and potential side effects.

3. Clinical Trials: Clinical trials are required to evaluate the safety and efficacy of quinoline-based anti-inflammatory agents in humans.

4. Structure-Activity Relationship Studies: Structure-activity relationship studies are necessary to understand the relationship between the chemical structure of quinoline derivatives and their pharmacological activities.

5. Toxicity Studies: Comprehensive toxicity studies are needed to fully assess the potential side effects of quinoline-based anti-inflammatory agents.

By pursuing these research avenues, scientists and clinicians can work together to develop new and innovative treatments for inflammatory diseases, ultimately improving human health and quality of life.

REFERENCES

[1] Am. J. Antimalarial Drug Resistance: Literature Review and Activities. 2015; 93(3): 57–68.

[2] Murray CJ, Rosenfeld LC, Lim SS, Andrews KG, Foreman KJ, Haring D, Fullman N, Naghavi M, Lozano R, Lopez AD. Global malaria mortality between 1980 and 2010: a systematic analysis. 2012; 379: 413–431.

[3] Anstey NM, Sugiarto P, Warikar N, Kenangalem E, Karyana M, Lampah DA, Price RN. Multidrug-resistant Plasmodium vivax associated with severe and fatal malaria: a prospective study. 2008; 5(6): 128.

[4] Gosling RD, Okell L, Mosha J, Chandramohan D. The role of antimalarial treatment in the elimination of malaria. 2011; 1(17): 1617–1623.

[5] Joaniter nankabirwa, simon j. Brooker, sian e. Clarke, deepika, fernando, fernando, caroline w. Gitonga, david schellenberg, brian greenwood. Malaria in school-age children in a frica: an increasingly important challenge. 2014; 11(19): 1294-1309.

[6] Macdonald, G. The epidemiology and control of malaria. 1957.

[7] Russell, P. F., L. S. West, R. D. Manwell, and G. Macdonald. Practical malariology. 1963; 44: 372.

[8] Gabald on, A. Malaria incidence in the West Indies and South America. 1949: 764-7987.

[9] Gill, C. A. The seasonal periodicity of malaria and the mechanism of the epidemic wave. 1938.

[10] Maria Anice Mureb sallumeduardo Sterlino bergooswaldo Paulo Forattini. First Record of Anopheles benarrochi Gabaldon, Cova Garcia & Lopez from the State of São Paulo, Southern Brazil. 1997; 92(2): 233-234.

[11] Giglioli, G. The influence of geological formation and soil characteristics on the distribution of malaria and its mosquito carrier.1951; 39: 48-56.

[12] WHO, World Health Organization. Report of the informal consultation on stratification for planning antimalaria action. 1985: https://apps.who.int/iris/handle/10665/61393.

[13] WHO, World Health Organization. National malaria control and scaling up for impact: the Zambia experience.2006: http://www.rollbackmalaria.

[14] S. I. Hay, C. A. Guerra, A. J. Tatem, A. M. Noor, R. W. The global distribution and population at risk of malaria. 2004; 4: 327-336.

[15] K. Rowe, S. Y. Rowe, R. W. Snow, E. L. Korenromp, J. R. M. Armstrong Schellenberg, C. Stein, B. L. Nahlen, J. Bryce, R. E. Black, R. W. The burden of malaria mortality among African children in the year 2000. 2006; 3(35): 691–704.

[16] R S Bray & P C C Garnham. Life-cycle of primate malaria parasites. 1982; 2(38): 117-122.

[17] G PASVOL, R J M WILSON,. The interaction of malaria parasites with red blood cells. 1982; 2(38): 133-140.

[18] H.E. Shortt, P.C.C. Garnham. Persisting Exo-erythrocytic Cycle in Plasmodium Cynomolgi. 1948; 1(26): 1225–1228.

[19] Grivennikov, S. I.; Karin, M. Inflammatory cytokines in cancer: tumour necrosis factor and interleukin 6 take the stage. Ann. Rheum. Dis. 2011, 70 (Suppl 1), i104.

[20] Kulagowski, J. J.; Baker, R.; Curtis, N. R.; Leeson, P. D.; Mawer, I. M.; Moseley, A. M.; et al. 3′-(Arylmethyl)- and 3′-(aryloxy)-3-phenyl-4 hydroxyquinolin-2(1H)-ones: orally active antagonists of the glycine site on the NMDA receptor. J. Med. Chem. 1994, 37 (10), 1402−5.

[21] Sharp, J. Antifungal methods employing certain carbostyrils. Patent US3836657A, 1974.

[22] Magedov, IV; Manpadi, M.; Ogasawara, M. A.; Dhawan, A. S.; Rogelj, S.; Van Slambrouck, S.; et al. Structural simplification of bioactive natural products with multicomponent synthesis. 2. Antiproliferative and antitubulin activities of pyrano[3,2-c]pyridones and pyrano[3,2-c]quinolones. J. Med. Chem. 2008, 51 (8), 2561−70.

[23] Kouznetsov, V.V.; Méndez, L.Y.V.; Gómez, C.M.M. Recent progress in the synthesis of quinolines. Curr. Org. Chem., 2005, 9, 141-161.

[24] Nayyar, A.; Jain, R. Synthesis and antituberculosis activity of 2, 4-disubstituted quinoline. Indian J. Chem., 2008, 47B, 117-128.

[25] Alam, M.M.; Sarkar, D.P.; Husain, A. Synthesis of quinoline-attached furan-2(3H)-ones having anti inflammatory and antibacterial properties with re duced gastro-intestinal toxicity and lipid peroxidation. J. Serb. Chem. Soc., 2011, 76, 1617-1626.

[26] Kandpal, B.; Meshram, J.; Mohanram, I.; Shaikh, A. Evaluation of newly synthesized quinazolinone de rivatives of hydrazones as potent anti-inflammatory and antibacterial agents. Med. Chem. Res., 2015, 24, 1419-1426.

[27] Wen, X.; Wang, S.B.; Liu, D.C.; Gong, G.H.; Quan, Z.S. Synthesis and evaluation of anti-inflammatory activity of quinoline derivatives. Med. Chem. Res., 2015, 24, 2591-2603.

[28] Detsi, A.; Bouloumbasi, D.; Prousis, K.C.; Koufaki, M. Design and synthesis of novel quinoline -3 aminoamides and their lipoic acid adducts as antioxi dant and anti-inflammatory agents. J. Med. Chem., 2007, 72, 50-54.

[29] Sekar, M.; Prasad, R.K.J. Synthesis of some novel 2 oxo-pyrano (2, 3-b) and 2-oxo-pyrido (2, 3-b) quino line derivatives as potential antimalarial, diuretic, clastogenic and antimicrobial agents. J. Chem. Tech nol. Biotechnol., 1998, 32, 50-54.

[30] Murti, Y.; Gupta, S.K.; Pathak, D. Synthesis, charac terization and antimalarial screening of some new N [(2-chloroquinolin-3-yl) methylene] benzenamines. Der. Pharma. Chemica., 2010, 4, 271-277.

[31] Magedov, I.V.; Manpadi, M.; Kornienko, A. Struc tural simplification of bioactive natural products with multicomponent synthesis 2. antiproliferative and anti tubulin activities of pyrano [3, 2-c] pyridones and pyrano [3, 2-c] quinolines. J. Med. Chem., 2008, 51, 2561-2570.

[32] Cope, H.; Mutter, R.; Heal, W.; Pascoe, C.; Chen, B. Synthesis and SAR study of acridine, 2 methylquinoline and 2-phenylquinazoline analogues as anti-prion agents. Eur. J. Med. Chem., 2006, 41, 1124-1143.

[33] Rajasekaran, A.; Rajamanickam, V.; Darlinquine, S. Synthesis, anti-inflammatory & analgesic evaluation of thioxoquinazolinone derivatives. Yakugakuzasshi, 2011, 7, 1079-1084.

[34] Azimvand, J. Synthesis of some new analogs of qui noline containing imine bond form the initial compo sition of aniline. J. Chem. Pharm. Res., 2012, 4, 3905-3908.

[35] Desai, N.C.; Harsora, J.P. Synthesis, characterization and antimicrobial screening of some quinoline based dihydro pyridine and 2-oxo-azetidine derivatives. In dian J. Org. Chem., 2012, 51B, 1001-101.

[36] Abhinav Prasoon Mishra, Preeti Verma and Riya Mathur, design, synthesis and evaluation of anti inflammatory, analgesic and anti pyretic activity of 7- amino quinoline derivatives, World Journal of Pharmaceutical Research, Volume 12, Issue 4, 798-825

[37] L. J. Cui, Z. F. Xie, H. R. Piao, K. Y. Chai, Z. S. Quan, Biol. Pharm. Bull. 2005, 28, 1216–1220.

[38] Z. S. Quan, J. M. Wang, J. R. Rho, K. C. Kwak, et al., Bull. Korean Chem. Soc. 2005, 26, 1757–1760.

[39] X.-Y. Sun, Y.-Z. Jin, L. Fu-Nan, L. Gao, et al., Arch. Pharm. Res. 2006, 29, 1080–1085.

[40] T. Ramalingam, M. S. Murty, Y. V. D. Nageswar, P. B. Sat tur, J. Heterocyclic. Chem. 1990, 27, 981–982.

[41] G. Chen, W. Shan, Y. Wa, L. Ren, et al., Chem.Pharm.Bull. 2005, 53, 1587–1590.

[42] Nathan, C. Inflammation: points of control. Nature, 2002, 420, 846-852.

[43] Thorlacius, H.; Xie, X. Histamine promotes leucocyte recruitment by prolonging chemo attractant-induced leucocyte adhesion in the rat mesentery. Acta Physiol. Scand., 1995, 155, 475-476.

[44] Sujeet Kumar Gupta1and Ashutosh Mishra, Synthesis, Characterization & Screening for Anti-Inflammatory & Analgesic Activity of

Quinoline Derivatives Bearing Azetidinones Scaffolds, Anti-Inflammatory & Anti-Allergy Agents in Medicinal Chemistry, 2016, 15, 31-43