Available online on 15.07.2022 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

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Review Article

The Chemical and Pharmacological Advancements of Quinoline: A Mini Review

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Article Info:

Article History:

Received 13 May 2022
Reviewed 28 June 2022
Accepted 04 July 2022
Published 15 July 2022

Cite this article as:

Bharti A, Bijauliya RK, Yadav A, Suman, The Chemical and Pharmacological Advancements of Quinoline: A Mini Review, Journal of Drug Delivery and Therapeutics. 2022; 12(4):PageNo.

DOI: http://dx.doi.org/10.22270/jddt.v12i4.5561

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Abstract

Quinoline is a preferred scaffold that emerges as a prominent assembly motif for the creation of novel pharmacological molecules among heterocyclic compounds. An important family of chemicals includes quinoline and its derivatives that have been studied for various biological activities. Due to its wide range of bioactivity, quinoline, which is made up of benzene fused with N-heterocyclic pyridine, has drawn a lot of interest as a key template in drug creation. In order to demonstrate the quinoline motifs' significant efficacies for upcoming drug development, this review intends to provide the most current developments in chemistry, their medicinal potential, and their pharmacological applications. As a result, these compounds have been produced by several scientific groups as intentional structures, and their biological functions have been examined. The current study offers succinct information on quinoline's natural sources, as well as details on newly marketed medications that include quinoline. The pharmacological effects of quinoline derivatives, such as their anticonvulsant, antibacterial, antiviral, anti-protozoal, antimalarial, anticancer, anti-inflammatory, and anthelmintic properties, are also discussed in this study.

Keywords: Nitrogen-Based Heterocycles, Quinoline, Synthesis, Biological Activities

INTRODUCTION:

Four out of the top five selling medications in the US are believed to include at least one heterocyclic molecule, which has pharmacological properties including antitumor, anticancer, antibacterial, and anti-inflammatory properties. Heterocyclic compounds are essential to many drug core structures as well as biological and pharmacological activities. [1] The relevant heterocycle in this review is quinoline, which is a prime example of a bicyclic heterocyclic molecule. A pyridine ring and a benzene ring fused with two nearby carbons make up the aromatic N-heterocyclic basic chemical known as quinoline. [2] Benzazine, benzo-pyridine, and benzo[b]pyridine are further names for it. [3] Leukol was the name given to the substance when it was first taken out of coal tar by Friedlieb Ferdinand Runge in 1834. The major source of commercial quinoline is still coal tar. [4] Later in 1842, Gerhardt isolated a compound and gave it the name quinoline by dry distilling quinine, strychnine, or cinchonine with alkali. [5]

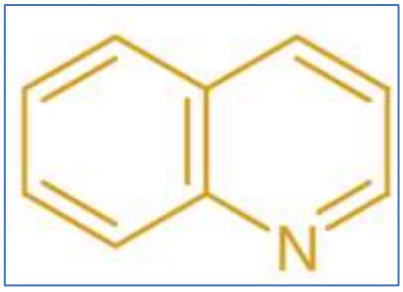


Figure 1: Quinoline Structure

The pKa of pure quinoline, also known as benzo [b] pyridine, in water at 20°C is 4.85. It is an oily, colourless, hygroscopic liquid. Its molecular weight is 129.16 and its chemical formula is C_9H_7N. It is exceedingly stable and frequently employed as a high-boiling solvent (b.p. 237 °C), albeit it darkens when exposed to light. The acidic pKa is 4.85 and the logP value is 2.04. A weak tertiary base is quinoline. With acids, it can form a salt and exhibits reactions akin to those of pyridine and benzene. Both nucleophilic and electrophilic substitution reactions are shown. [6, 7, 8]

Many naturally occurring physiologically active substances, such as quinine, chloroquine, bulaquine, primaquine, and tafenoquine from Cinchona alkaloids, include the quinoline core structure. [9] Typical drug design formulations make an effort to mimic naturally occurring heterocycles and exert potency by interfering with and interrupting the normal pathways required for the development of harmful organisms. Through their use as therapeutic agents, [10, 11, 12, 13] applications in human and veterinary medicine, [12] use in bioinformatics, [14] agriculture, [15, 16] polymers, [17] dyes, [18] and molecular engineering, [19] as well as their growing significance in numerous other fields, they have made a significant contribution to society.

NATURAL SOURCES OF QUINOLINES:

Quinoline may be obtained from a variety of natural sources, including animals, flowers, and microbes. Coal tar is the main source of quinoline. [21] Quinine, Quinidine, Cinchonine, and Cinchonidine are all found in Cinchona plant bark, which is compounded and used as "Quinimax" in the treatment of

malaria. [22] A dimethoxylated quinoline molecule called nitidine, an anticancer drug, is derived from the citrus plant Zanthoxylum nitidum. Reticuline, an isoquinoline, is found naturally in a number of well-known medicinal plants, including opium species, *Asimina triloba, Papaver somniferum*, and *Ocotea fasciculata*. Sedative and anticonvulsant medications include the furoquinoline alkaloid known as skimmianine, which is found in *Skimmia japonica*. *Nocardioides sp.* contains the substance sanamycin, which has anticancer and antibacterial properties. It is a biomolecule with two 2-amidoquinoline molecules in its central structure. [23] The bark and stem of the *Camptotheca acuminata* tree can be used to extract camptothecin (a pentacyclic quinoline). The Dictamnus species may be used to isolate quinoline alkaloids. For instance, the plant Dictamnus angustifolius is the source of the quinoline alkaloid robustine, while *Dictamnus albus* is the source of evolitrin, a tricyclic quinoline, *Dictamnus hispanicus* is the source of ribalinidine, and *Dictamnus dasycarpus* and *Dictamnus angustifolius* are the sources of dictamnine. [24]

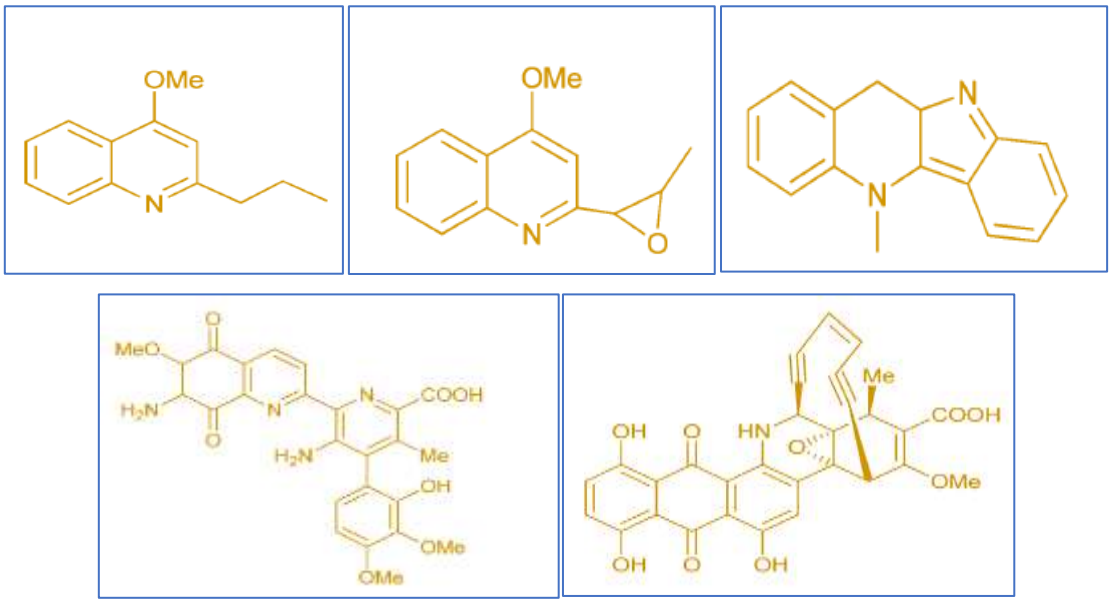
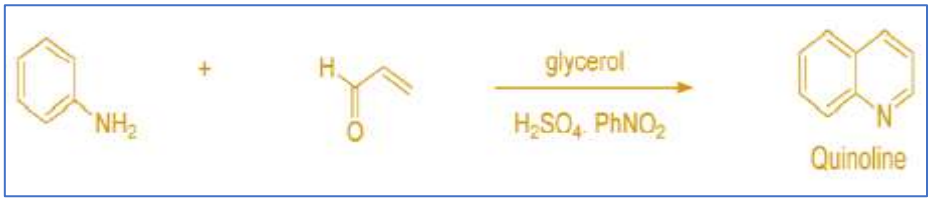


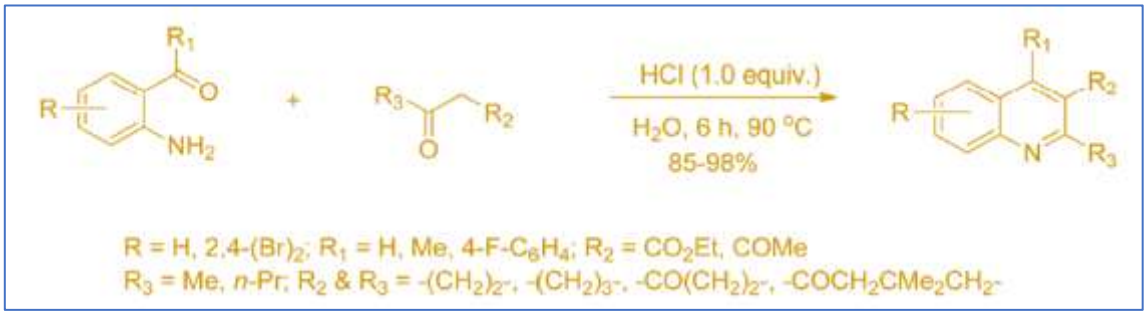
Figure 2: Quinoline derivatives isolated as natural products.

SYNTHESIS OF QUINOLINE DERIVATIVES

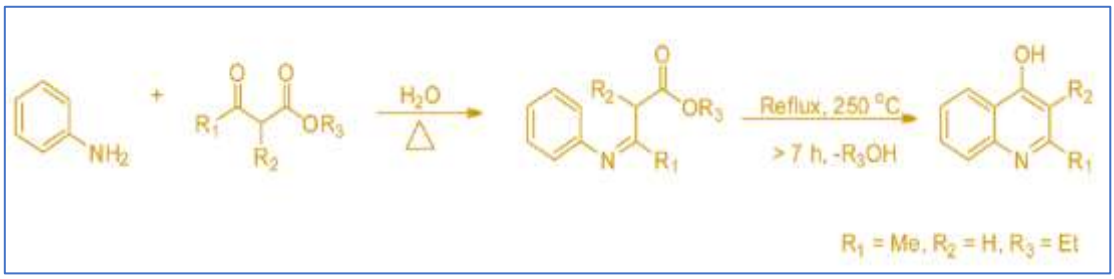
1. The Skraup synthetic approach: [25]



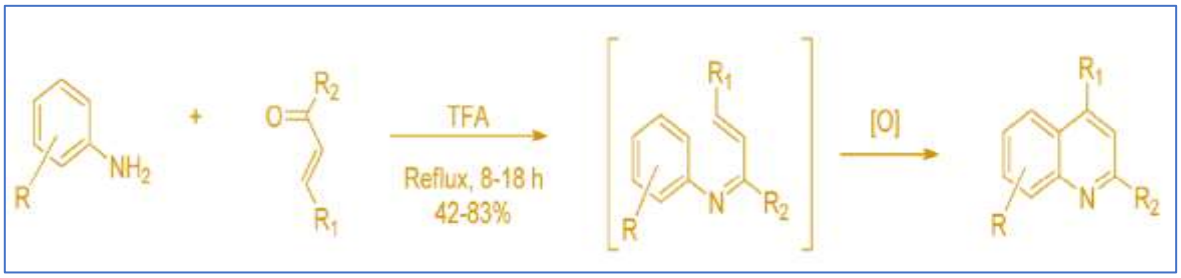
2. Friedlander Synthetic Approach: [26]



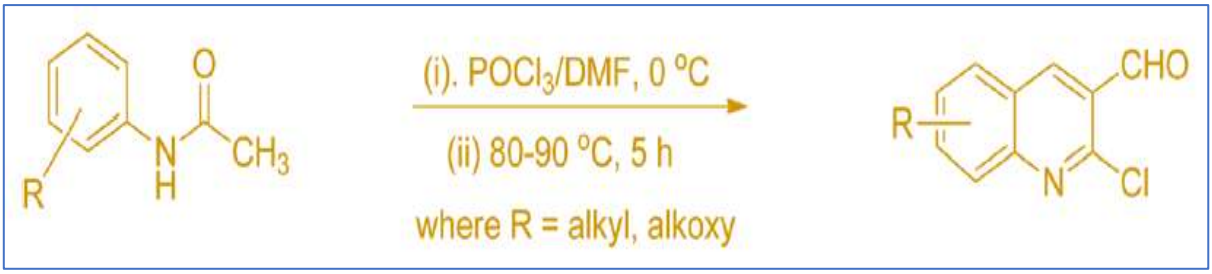
3. Conrad–Limpach synthetic approach: [27]



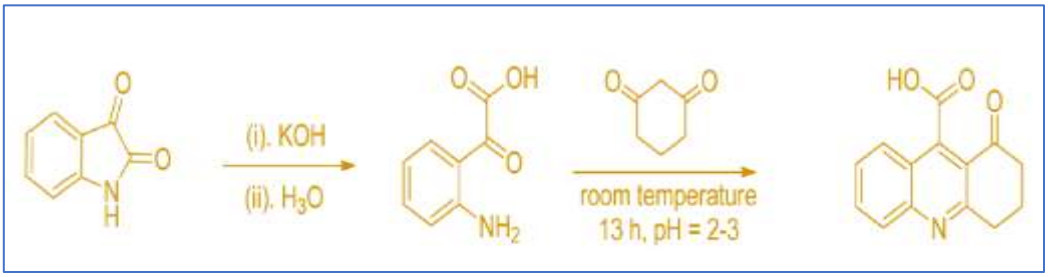
4. Doebner–Miller synthetic approach: [28]



5. Vilsmeier–Haack reaction: [29]



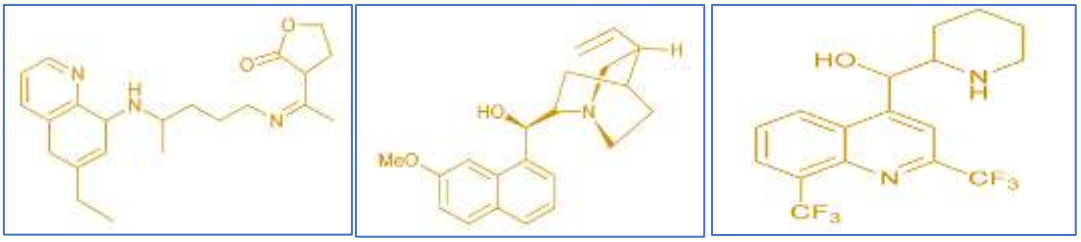
6. Pfitzinger synthetic approach: [30]



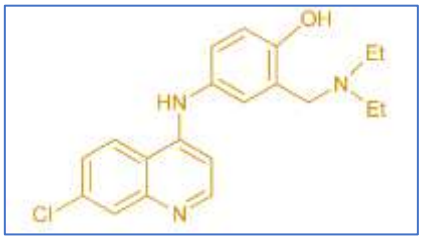
APPLICATIONS OF QUINOLINE AND ITS DERIVATIVES

In general, it is generally recognised that quinoline derivatives have a wide range of uses in synthetic organic chemistry, pharmaceutical chemistry, bioorganic chemistry, and industrial chemistry. Numerous biological actions, including anti-malarial, anti-bacterial, anti-fungal, anti-asthmatic, anti-hypertensive, anti-inflammatory, and antiplatelet activity, have been discovered in their derivatives. [31] Additionally, they have anti-tubercular and immune-depressing properties. Some quinoline-ringed substances are showing promise as antimalarial medications, such as pamaquine, chloroquine, tafenoquine, bulaquine, quinine, and mefloquine, as well as amodiaquine, which has antimalarial and anti-inflammatory properties. [32-36] The oestrogen receptor b (ER b), which is crucial for the growth, upkeep, and operation of the mammalian reproductive system as well as in non-sexual tissues, is selectively binded to by the 2-arylquinoline derivatives. [37]

Pamaquine Chloroquine Tafenoquine



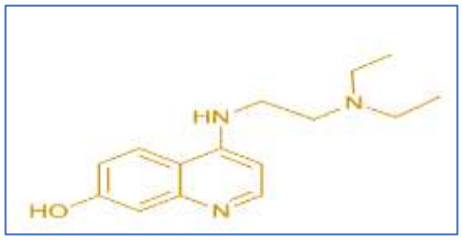
Bulaquine Quinine Mefloquine



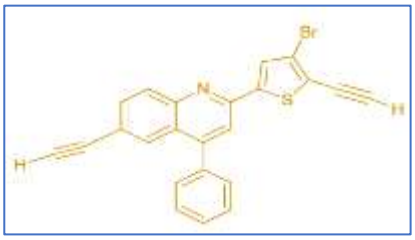
Amodiaquine

2-arylquinoline derivatives a) and b)

Nitrogen at position 4 of 4-[2-(Diethylamino) ethylamino] quinolin-7-ol results in antiplasmodial action. [38] Metal complexes that emit light have been created using polysubstituted quinoline derivatives such 8-hydroxyquinoline and quinoline-8-thiol. [39] Sensors and light-emitting diodes have used 2-(4-Bromo-5-ethylnylthiophen-2-yl)-6-ethynyl-4-phenylquinoline. [40]



4-[2-(Diethylamino) ethylamino] quinolin-7-ol

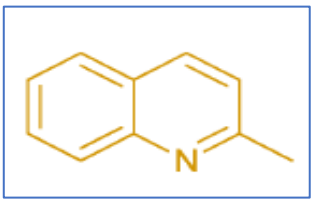


2-(4-Bromo-5-ethylnylthiophen-2-yl)-6-ethynyl-4-phenylquinoline

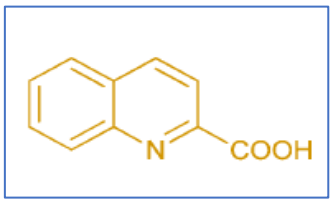
With noticeable differences depending on the pattern of substitution, a novel family of hybrid conjugates of N-(7-chloroquinolin-4-yl) piperazine-1-carbothioamide and 1, 3, 5-triazine derivatives have significant antimalarial activity against both wild and mutant parasites. Against a variety of gram-positive and gram-negative pathogens, these compounds also exhibit remarkable antibacterial activity. [41, 42]

The pathogenic parasite Toxoplasma gondii is resistant to the antiprotozoal effects of derivatives of 4-arylquinoline-2-carboxylate. [43] Numerous quinoline derivatives have been shown to be useful as agrochemicals [44] and in the research of bio-organic and bio-organometallic processes. [31] Additionally, they are employed in the production of organic molecules such as pH indicators, food colouring, and dyes. They have furthermore been employed as ligands to create OLED phosphorescent complexes [45] and with conjugated polymers as selective chemo-sensors for metal ions and fluoride. [46, 47]

In hydrochloric acid, several quinoline derivatives, including quinalidine and quinaldic acid, have action as corrosion inhibitors for mild steel. [32] Recent years have seen the development of new Raf kinase inhibitors with more powerful and focused anticancer activity from quinoline derivatives that examined the structural alteration of sorafenib. [48] Strong antiplasmodial action is displayed by aziridine-isoquinoline combinations and their ring-opening derivatives. [49]



Quinalidine



Quinaldic Acid

CONCLUSION:

In the realm of medication research and discovery, quinoline and its analogues are extremely notable heterocyclic molecules. They represent a highly important class of scaffolds that are potentially found in nature and have a considerable impact on medicinal chemistry. The use of quinoline derivatives as therapeutic molecules to treat different diseases and infections has drawn increasing attention. From a current perspective, this is essential because we require an ecologically sound technique for the mass manufacture of a crucial biological component that can then be employed in a variety of processes to create an effective pharmacophore in the future.

ACKNOWLEDGEMENT:

The author is thankful to Mr. Rohit Kumar Bijauliya, Assistant Professor, BIU College of Pharmacy, Bareilly International University, Bareilly for their valuable guidance.

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