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Review Article

Quinoline-A Next Generation Pharmacological Scaffold

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ABSTRACT

QUINOLINE is a nitrogen containing heterocyclic aromatic compound which has a molecular formula C7H9N.Quinoline compounds are found in various natural resources like quinine (antimalarial), camptothecin (belotecan) anticancer drug .Quinoline is considered an important biological active moiety with numerous biological properties such as antimalarial, antibacterial, anti-inflammatory ,anti-arrhythmic anti-anginal, anti-depressant, antihypertensive, antituberculosis, anticonvulsant, antifungal, anti -leishmanial, antidiabetic, antioxidant, antimicrobial ,anticancer ,antiviral ,CVS diseases ,anti-HIV ,and anti -helminthic ,local anesthesia anti-asthmatic and its derivatives used in various neurological disorders like Alzheimer's and CNS disorders.

INTRODUCTION

Quinoline was first isolated by Runge in 1834 from coal tar. Coal tar also contains isoquinoline, alkyl quinolines and alkyl isoquinolines. Quinoline consists of benzene ring fused to α and β positions of pyridine ring hence derives its other name is Benzo pyridine, benzo azabenzene.[1]

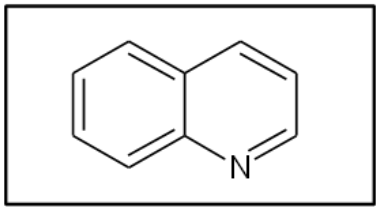

Figure:1 Structure of quinoline

AROMATICITY OF QUINOLINE:

Quinoline is an aromatic heterocycle formed by the fusion of a benzene and a pyridine ring. It is a planar molecule with all atoms sp^2 hybridized, allowing continuous π-electron delocalization that satisfies Hückel's rule (4n + 2).[2]

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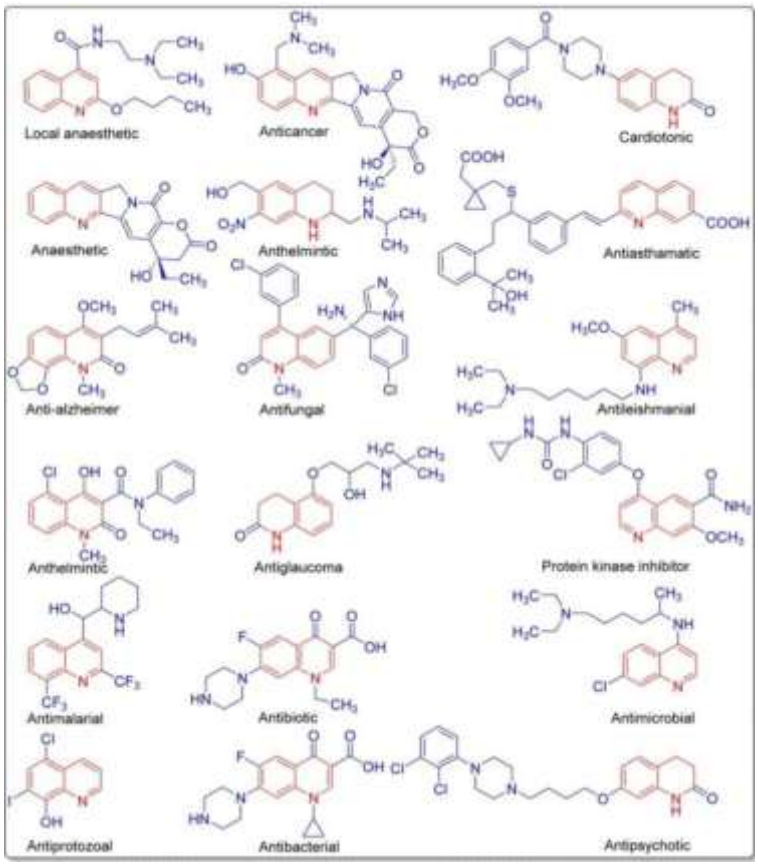

Figure: 2 Quinoline containing nucleus with different pharmacological activity [3]

Pharmacological activities of Quinoline and its derivatives:

ANTI-MALARIAL ACTIVITY:

M. Touré et al. (2025) reported chloroquine–isatin hybrids with structural variations in the isatin moiety and linker to the 7-chloroquine core. These compounds showed strong activity against Plasmodium falciparum, likely by inhibiting hemozoin formation. A newly synthesized aminoquinoline derivative exhibited high potency against the chloroquine-sensitive Pf3D7 strain with an of 0.25 μM, demonstrating significant antimalarial potential. [4]

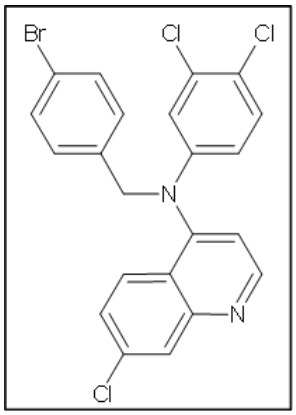

Figure :3 Quinoline derivative having anti - malarial activity

ANTI-CANCER ACTIVITY:

Ameen Ali Abu-Hashem et al. (2024) conducted a systematic study on anticancer quinoline derivatives, classifying them into scaffold-based groups such as quinoline-chalcones, quinoline-thiazoles, and quinoline-urea's for clear SAR analysis. Electron-donating groups at the para position enhanced antiproliferative activity against

MCF-7, HeLa, and A549 cell lines, while electron-withdrawing groups showed variable effects. Among the synthesized compounds, 8- phenyl-6-(quinolin-2-yl)-11H-pyrido(3,2:5,6)pyrimido(2,1-b:4,3-b)diquinazoline-11,18-dione exhibited particular activity against MCF-7. [5]

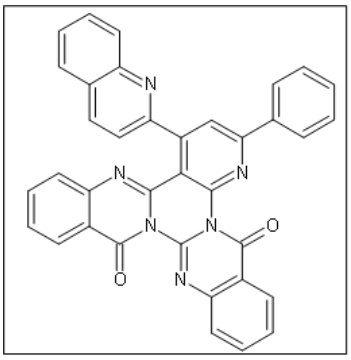

Figure: 4 Quinoline derivative having anti-cancer activity

ANTI TUBERCULAR ACTIVITY:

Zaheer et al. prepared the novel compounds N-(2-Chloro-6 isomethoxyquinolin-3-yl) methyl) isonicotinohydrazide and N-(2-chloro and N-(2-chloro-6-methoxyquinolin-3-yl) -3-fluro-4-morpholino aniline by 4-methoxy acetanilide which is reacted with POCl3 at 80ºc to give 6-methoxy 2-chloroquinoline-3-carbaldehyde through the Vilsmeier-Haack reaction. These compounds exhibited exceptional activity against MTB with MIC value of 15.00µm [6]

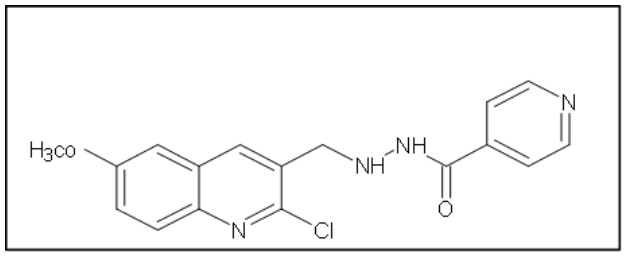

Figure :5 Quinoline derivative having anti -TB activity

ANTI-DIABETIC ACTIVITY:

Quinoline-based hybrids 1-(7-chloroquinolin -4-yl)-1H-pyrazolo[3,4-d] pyrimidin-4-amines and 7-chloro-N-phenylquinolin-4-amine were synthesized and evaluated for their glucosidase inhibitory and anti-oxidant properties IC50=46.70and 40. 84µM, compared to the reference inhibitor acarbose IC50=51.73µM. [7]

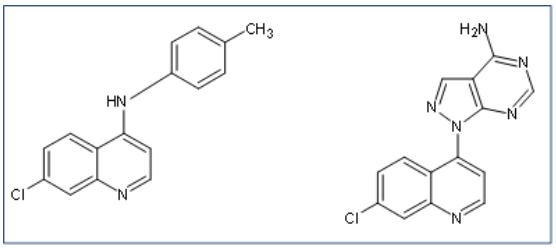

Figure :6 Quinoline derivatives having anti-diabetic activity

ANTI-LEISHMANIAL ACTIVITY:

Silva et al.(2023) developed a series of 1,2,3,4-tetrahydroacridine derivatives through virtual screening against S-adenosylmethionine decarboxylase and evaluated their activity against Leishmania infantum promastigotes. A structure–activity relationship (SAR) study revealed that the alkyl chain length strongly influenced antileishmanial activity, particularly in dimeric compounds. However, due to the high toxicity associated with the tetrahydro acridine scaffold, the researchers replaced it with a 7-chloroquinoline core, which retained potent antileishmanial activity while significantly reducing toxicity [8]

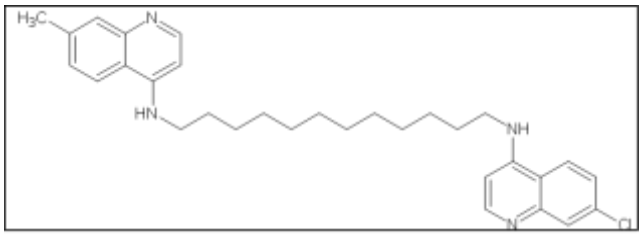

Figure:7 Quinoline derivative having anti-leishmania activity

ANTI-HIV ACTIVITY:

Quinoline-1,2,3-triazole-aniline hybrids were synthesised in moderate to good yields promising

in vitro activities against the wild-type HIV-1 subtype B, with AZT (IC50 = 0.0909 µM), the reference drug. Furthermore, compound displayed moderate activity, with a MIC90 of 88µM against Mtb's H37Rv strain. Cytotoxicity studies on TZM-bl cell lines revealed that most of the tested compounds were generally non-cytotoxic; the selectivity index (SI) for the front runner, is >2472. Molecular docking studies revealed that 11h interacted with Phe112, Tyr108, Glu283 and Trp86 amino acid residues in the active site of HIV-1. DFT studies revealed that 11h has the ability to donate and accept electrons to and from available orbitals. The predicted ADMET studies showed that these compounds possess drug-likeness, and has the potential an anti-HIV-1 agent.[9]

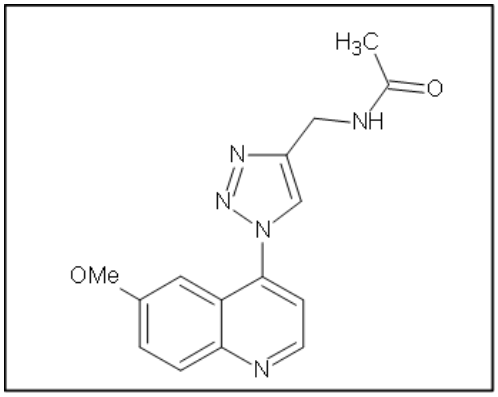

Figure: 8 Quinoline derivative having anti-HIV activity

ANTI-INFLAMMATORY ACTIVITY:

The bioactiveN1-(5-methyl-5H-indolo[2,3-b] quinoline-11-yl) benzene -1,4-diamineHCL was synthesized, with different concentrations (50mg,100mg,200mg). And naturally occurring plants also have anti-inflammatory activity; Cryptolepis sanguinolenta, the roots of this shrubs used as medicine, and it contains indoloquinoline alkaloids. These alkaloids are formed by the fusion of indole and quinoline with different sites and orientation. Neocryptolepine and its region isomer cryptolepine have potent anti-inflammatory and cryptolepine has been demonstrated to reduce nitric oxide generation.[10]

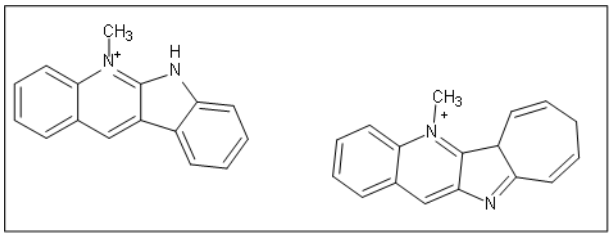

Figure: 9 Quinoline derivatives having anti-inflammatory activity

ANTI-HELMINTHIC ACTIVITY:

The anti -helminthic activity of quinoline based compounds report the synthesis and evaluation of novel quinoline derivatives with anti-parasitic effect. One notable study 2024, study synthesized and tested new thiosemicarbazide and 1,2,3-triazole quinoline derivatives for their anti-helminthic activity, demonstrate potential effectiveness against parasitic worms. [11]

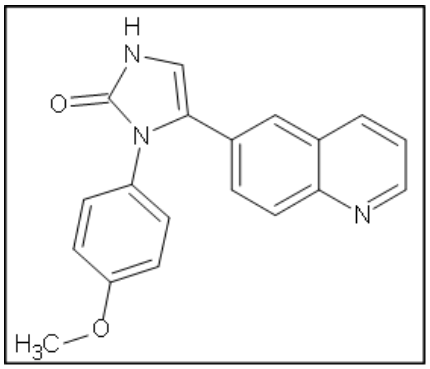

Figure:10 Quinoline derivative having anti-helminthic activity

ANTI-VIRAL ACTIVITY:

Kutkat et al. synthesized a novel series of 1,2,3-triazole glycosides that displayed either antiviral activity of benzoxazole, benzimidazole, benzotriazole, was protective against H1N1 infection.To discover novel anti-viral agents, based on high anti-viral activity of (4- oxo-4H-quinolin-1-yl)- acetic acid hydrazide. Quinoline tricyclic derivative exhibited anti- HCV

(hepacivirus) EC50=3.1µm and anti-BVDV EC50=1.2µm.[12]

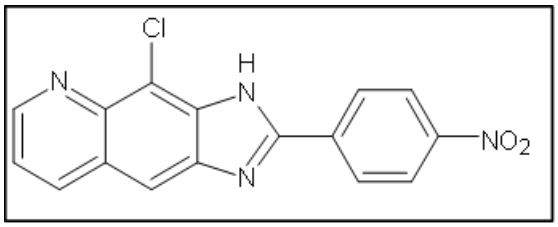

Figure: 11 Quinoline derivative having anti-viral activity

ANTI-MICROBIAL ACTIVITY:

VK Singh et al. (2024) designed and synthesized new quinoline derivatives functioning as peptide deformylase inhibitory and fungal cell wall disruptors. The synthesis of quinoline derivatives starting from 6-amino-4-methyl-1H-quinoline-2-one substituted with different types of sulfonyl moieties. These newly synthesized compounds were evaluated for their anti-bacterial activity. Antibacterial screening of all compounds showed excellent MIC value (MIC,50-3.12µg/mL) against bacterial strains of Bacillus cereus, staphylococcus, pseudomonas, E.coli. [13]

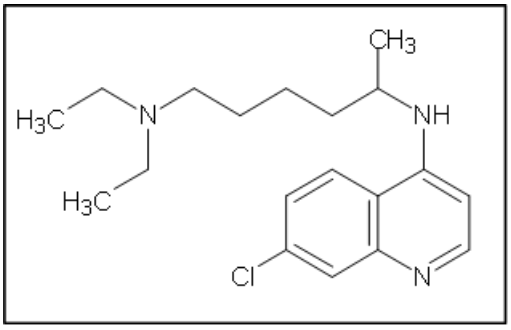

Figure:12 Quinoline derivative having anti-microbial activity

LOCAL ANESTHETIC ACTIVITY:

In 2023, Azamatov, Zhurakulov, and Vinogradova from the Institute of Chemistry of Plant Substances synthesized and evaluated 1-aryltetrahydroisoquinoline derivatives, quinoline analogues, for local anesthetic activity. Centbucridine, a potent quinoline derivative, exhibits strong antihistaminic, vasoconstrictive, and anesthetic effects 4–5 times more effective than lignocaine and is used in dentistry and ophthalmology by blocking sodium channels to inhibit nerve impulse conduction and induce local anesthesia.[14]

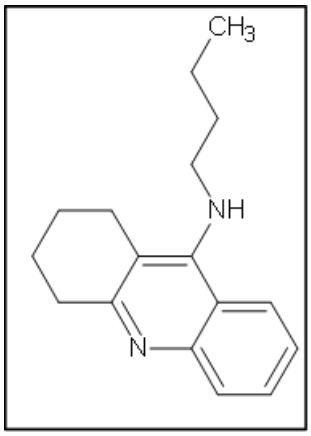

Figure: 13 Quinoline derivative having local anesthetic activity

ANTI-HYPERTENSIVE ACTIVITY:

Inhibition of angiotensin converting enzyme (ACE) is identified as a main therapeutic target in controlling hypertension. The principal intent of this is to investigate the ACE inhibitory property of quinoline appended chalcone derivative(E) -3-(anthracene-10-yl) -1-(6,8- dibromo-2-methylquinolin-3-yl) prop-2-en-one and its binding mechanism with model transport protein by employing steady state and time resolved In-silico molecular model. [15]

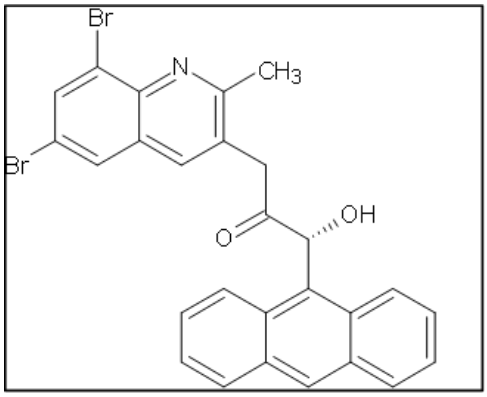

Figure: 14 Quinoline derivative having anti-hypertensive activity

ANTI-CONVULSANT ACTIVITY:

Challal et al. 2023 investigate the structural similarities between conventional small molecule antiseizures and natural alkaloids, which are nitrogen containing organic compounds commonly present in plants. These alkaloids have been historical recognized for their pharmacological effects including neuroprotective action.[16]

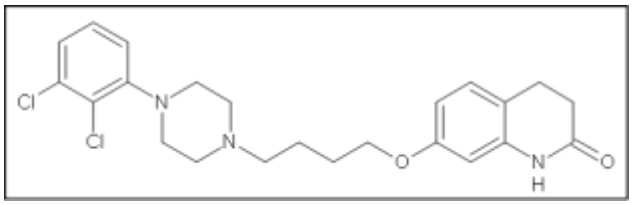

Figure: 15 Quinoline derivative having anti-convulsant activity

CONCLUSION:

Quinoline derivatives and their hybrids serve as vital structural scaffolds in medicinal chemistry, underpinning the design of therapeutically effective molecules. Their structural versatility and broad biological activities make them privileged frameworks in modern drug discovery. Identifying moieties that enhance activity when hybridized with quinoline remains key to developing novel therapeutics. Continued optimization of quinoline-based structures is expected to produce innovative drugs addressing unmet medical needs across diverse diseases, reaffirming quinoline's central role in pharmaceutical research.

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