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Review Article

QUINOLINE SCAFFOLD – A MOLECULAR HEART OF MEDICINAL CHEMISTRY

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Quinoline is the most important structure in the series of Heterocyclic compounds that give the different activities such as antibiotic, anti-inflammatory, analgesic, antimalarial, antidiabetic, anticancer etc of them are under evaluation in clinical trials. In the antibiotic activity, there are 3 new quinolone cognates that were primed through alkylation of 2-oxo-1,2-dihydroquinoline-4-carboxylic acid with the ethyl-2-Bromoacetate. Different spectroscopy for most of the activities like mass spectroscopy, NMR, IR, etc.

Keywords: Quinoline, a heterocyclic compound, biological activities,

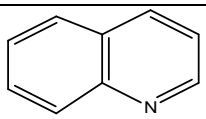
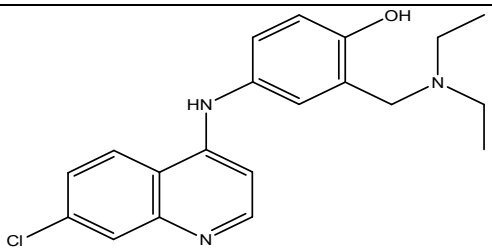
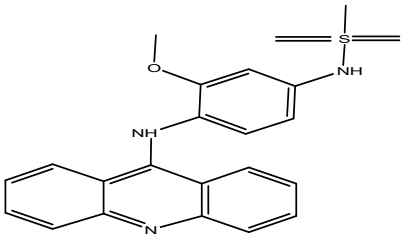
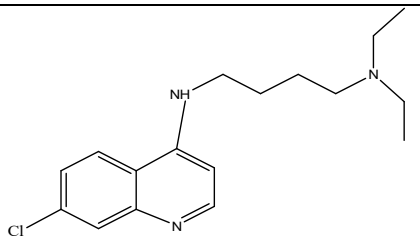
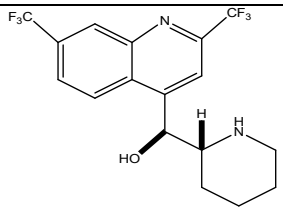
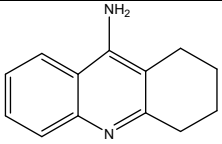
INTRODUCTION

1) By the definition, Heterocyclic compounds are those that contain a minimum of one Heteroatom (i.e. Nitrogen,sulphur, oxygen) in cyclic ring.Carbocyclic compounds are cyclic chemical compounds that contain all carbon atoms in the ring formation.Quinoline is the most important compound in the series of Heterocyclic Aromatic Compounds with Industrial and Medical Applications. It has a two-ring structure containing one benzene ring that is fused together pyridine nucleusBecause of their utility for manyHeterocyclic scaffolds, particularly those containing nitrogen heterocyclic compounds, play a significant influence in the design of new due of the medications they have a high degree of the tendency for linking.(4)Compounds contain the quinoline nucleus and also are regarded for medicinal activities [1] Quinoline nuclei have been known since 1962. Different pharmacological qualities that are exceptional (2) Such as Antimalarial, Antibiotics, Antioxidant, Antifungal, Anti-inflammatory etc.The quinoline alkaloids are especially determined in plants, such as Rutaceae and Rubiaceae, but also in microorganisms and animals. introducing additional functional groups to the quinoline scaffold is a great idea for novel medication development.(3)Many publications have been written about quinoline [1] and its derivatives' synthesis.,Chloroquine, for example, is an immunostimulant having a 4-aminoquinoline Skelton.(5),Amodiaquine[2], Amsacrine, Chloroquine, Mefloquine, Cinchonine, Chinchonidine, Quinine, Tacrine structure as shown in **Table 1**

ISSN 2249-3875

International Journal of Pharmaceutical Erudition

Table-1: Chemical structure of different molecules

1.		Quinoline
2.		Amodiaquine
3.		Amsacrine
4.		Chloroquine
5.		Mefloquine
6.		Tacrine

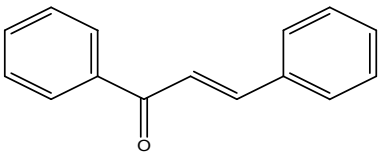
ISSN 2249-3875

International Journal of Pharmaceutical Erudition

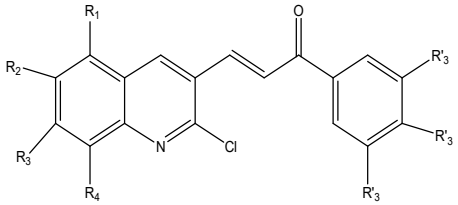
2. Biological Activity of Quinoline Derivatives

2.1. Anticancer activity:

Cancer is a huge life-threeatening disease to protect human well-being around the world, as 12 million individuals have already been diagnosed with it and seven million people have died as a result of it.([6])SalimehMirza*et al.* (2020). a novel quinoline-chalcone family was created in hybrids **1**.Different spectroscopic approaches were used to characterise the structures of these substances. including IR, UV and 13C-NMR and mass-spectroscopy Humanovariancarcinomas and Cisplatin-resistant human ovarian carcinoma, human breast cancer cells, Mitoxantroneresistant human breast cancer cells, and normal Huvec-cells were used to assess the cytotoxic activities of drugs. This paper discusses the SAR of produced chemicals.In the quinoline chalcone hybrid, 2 different substitutionsin different positionsshowa different level of activity Amongquinolines ([7])



Chalcone



Quinoline-Chalcone hybrid

Among these substituted quinoline charcoal hybrid compounds 2a,2b, and 2c show Both resistant cancer cells and their parents demonstrated high cytotoxic activity. And compounds 2b and 2c demonstrated the highest antiproliferative efficacy at half-maximal inhibitory concentration values. They were also discovered to be tubulin inhibitors, causing apoptosis as well as In the G2/M phase, the cell cycle stops.

2.2. Antibiotic Activity:

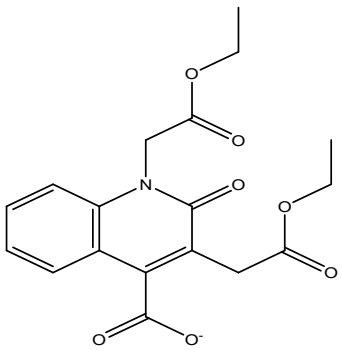
The ineffective antibiotic medication causes millions of deaths annually due to bacterial infections. Bacterial-resistance to conventional antibiotics complicates the situation. ([8])In Yusuf Sert b et al., Three novel quinolone derivatives have been discoveredby alkylation of 2-oxo-1,2—dihydroquinoline-4-carboxylic acid with ethyl-2-bromoacetate. They synthesized three

Compounds	X_1	x_2	x_3	x_4	x'_1	x'_2	x'_3
2a	COPh	H.	H.	H.	H.	OCH_3.	H.
2b	H.	H.	COPh.	H.	H.	OCH_3.	H.
2c	COPh	H.	H.	H.	OCH_3.	OCH_3.	OCH_3.

ISSN 2249-3875

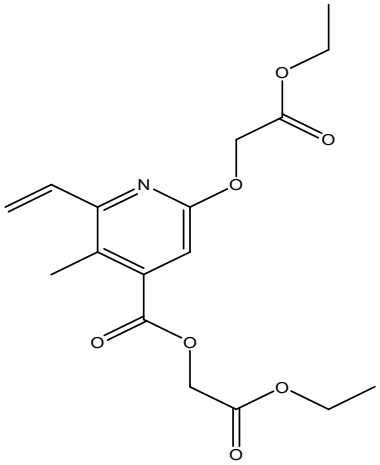
International Journal of Pharmaceutical Erudition

compounds which are mentioned in figures[Fig:3a], [Fig: 3b], and [Fig: 3c].which were characterized by using different spectroscopy methods. The crystal structure of Ethyl-1-(2-ethoxy-2-oxoethyl)-2-oxo-1,2-dihydro-1-quinoline-4- carboxylatewas determined by single-crystal X-ray diffraction. The optimized structures of 2-ethoxy-2-oxoethyl 1-(2-ethoxy-2-oxoethyl)-2-oxo-1,2- dihydro-1-quinoline-4-carboxylate, 2-ethoxy-2-oxoethyl 2-(2-ethoxy-2-oxoethoxy)quinoline-4-carboxylate, Ethyl-1-(2-ethoxy-2-oxoethyl)-2-oxo-1,2-dihydroquinoline-4-carboxylate in gas phase, The chemical shifts of 1H and 13C-NMR, the molecular electrostatic potential (MEP), frontier orbitals, and non-linear properties (NLO) have all been studied. Antibacterial activity of all substances was tested in vitro against bacterial strains of Pseudomonas pyocyanin, Escheerichiaa colie, Streptococcus faecaaliis, and Stephyllococcus aureeus([9])



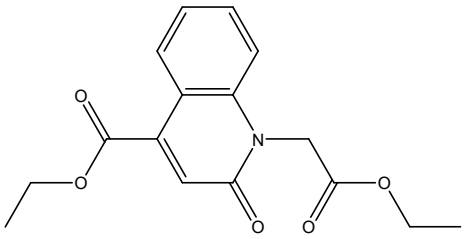
2-ethoxy-2-oxoethyl-1-(2-ethoxy-2-oxoethyl)-2-oxo-1,2,-dihydroquinoline-4-carboxylate

3a



2-ethoxy-2-oxoethyl 2-(2-ethoxy-2-oxoethoxy)-4- carboxylate quinoline

3b



Ethyl-1-(2-ethoxy-2-oxoethyl)-2-oxo-1,2-dihydro-1-quinoline-4-carboxy

3c

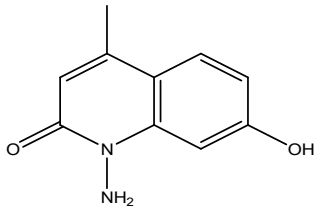
2.3. Antimalarial activity:

Malaria remains one of the most dangerous infectious diseases on the planet. Given the increased prevalence of antimalarial resistance, the development of novel and effective antimalarials remains a top goal. Malaria is a conceivably lethal tropical ailment transmitted from one person to another by mosquitos and a result by Plasmodium protozoan -parasites.

ISSN 2249-3875

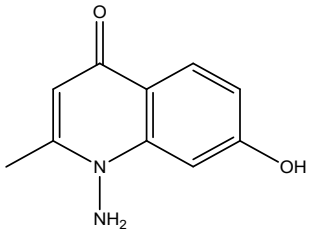
International Journal of Pharmaceutical Erudition

Plasmodium falciparum is the parasite that causes cerebral.malaria, is the most serious formof the disease, and it is responsible for the majority of the 1million deaths linked to malariaeeach year.([11]) According to Sanjay Kumar Vishwakarma *et al.*(2021)Schiff bases of 1-amino7-hydroxy-4- methyl quinoline-2(aH)-one [Fig: 4a]and 1-amino7-hydroxy-2-methyl quinoline-4(1H)- one[Fig:4b] with substituted aromatic carbonyl compounds were synthesized([12]) and the final yield is characterized by different techniques of spectroscopy such as Mass spectroscopy, IR spectroscopy, and 1HNMR.



1-amino-7-hydroxy-4- methylquinoline-2(1H)-one

4a

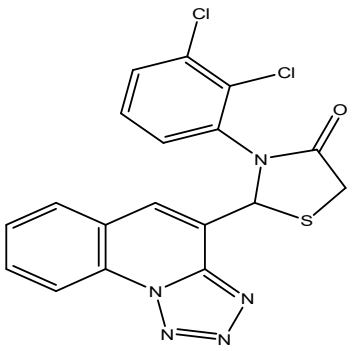


1-amino-6-hydroxy-2-methyl-1-quinoline-4(1H)-one

4b

2.4. Analgesic Activity:

Analgesics are medications that reduce or eliminate pain associated with a variety of pathologic diseases. ([13])as per the paper of Sujeet kumar Gupta *et al.*(2016).Some novelthiazolidine-1-ones substituted quinoline derivatives such as 3(2,3-dichlorophenyl)-2(tetrazolo[1,5-a]quinolin-4- yl)thiazolidin-4-one, 3-(3,4-dichlorophenyl)-2-(tetrazolo[1,5-a]quinolin-4- yl)-thiazolidin-4-one, 3-(3-fluorophenyl)-2-(tetrazolo-[1,5-a]quinolin-4-yl)thiazolidin-4-one, 3-(2-hydroxyphenyl)-2-(tetrazolo-[1,5-a]quinolin-4-yl)thiazolidin-4-one, 3-(3-hydroxyphenyl)-2-(tetrazolo[1,5-a]quinolin-4-yl)thiazolidin-4-one, 3(4-hydroxyphenyl)-2-(tetrazolo[1,5-a]quinolin-4- yl)thiazolidin-4-one, 3-(2-mercaptophenyl)-2-(tetrazolo[1,5-a]quinolin-4- yl)thiazolidin-4-one have been analgesic activities and In Vilsmeier-Haack reagent (N,N-Dimethylformamide + Phosphoroxidchlorid) react with acetanilide

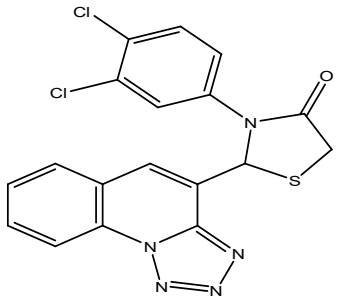


3-(2,3-dichlorophenyl)-2-(tetrazolo,[1,5-a]quinolin-4- yl)thiazolidin-4-one

5a

ISSN 2249-3875

International Journal of Pharmaceutical Erudition



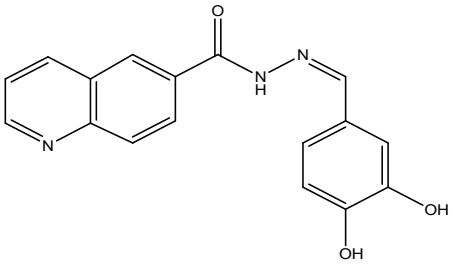
3-(3,4-dichlorophenyl)-2-(tetrazolo,[1,5-a]quinolin-4- yl)thiazolidin-3-one

5b

about 8-9 hrs to form2- chloro-3-formyl quinoline. Then 2- chloro-3-formylquinoline was treated with p-toluene sulphonic acid (PTSA) and sodium azide (NaN_3) to give the tetrazolo[1,5-a],quinoline4-carbaldehyde.

2.5. Antidiabetic activity:

Muhammad Taha *et al*.2019 reported by synthesising 25 compounds based on Schiff base reaction,Under positive control acarbose, twenty-five analogues for quinolinebased Schiff bases were tested as inhibitors of the α-glucosidase enzyme.when observe the activity profile he found that derivative 1,2,3,4,11,12, and 20 show the half-maximal inhibitory concentration value is (12.40 ± 0.40, 9.40 ± 0.30, 14.10 ± 0.40, 6.20 ± 0.30, 14.40 ± 0.40, 7.40 ± 0.20 and 13.20 ± 0.40 µM) and derivative 4 (IC50 = 6.20 0.30 M) was shown to have more times greater inhibitory action against glucosidase than the reference medication in this study. Eight derivatives (5, 7, 8, 16, 17, 22, 24, and 25) showed less than 50% inhibition in the entire series.[14]

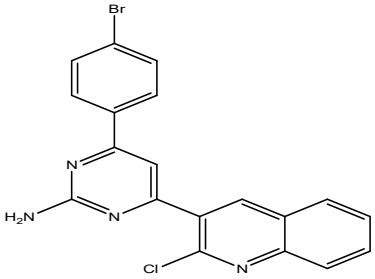


(Z)-N-(3,4-dihydroxybenzylidene)quinoline-6-carbo-1-hydrazide **[Derivative – 4]**

6a

2.6 Anti-HIV activity:

Nivedita Bharadwaj. *et al*. (2020) reported that quinoline derivatives are effective inhibitorsviral RNA to double-stranded viral DNA. In this research 11 derivatives are synthesized which are docked on a binding site for HIV reverse transcriptase. Among the 11 compounds, most of the compounds showthe best binding interaction with the action domain of the receptor. Compound 4 [4-(4-Bromophenyl)-6



4-(4-bromophenyl)-6-(2-chloroquinoline-3yl) pyrimidine-2amine **[Derivative- 4]**

7a

ISSN 2249-3875

International Journal of Pharmaceutical Erudition

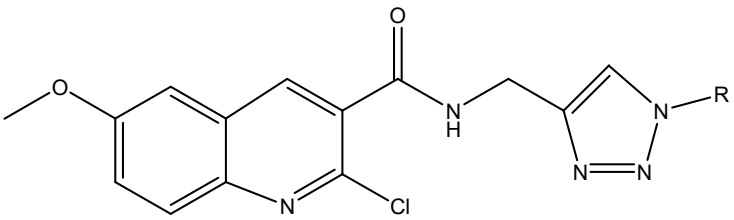
-(2-chloro,quinoline-3yl) pyrimidine-2-amine]had the best docking score of all the produced quinoline derivatives. [15]

2.7 Anti SARS Cov-2:

2019 coronavirus disease is the name given to the SAARS-CoV-2 is a a pathogen that causes sickness (COVID-19) [16]2019 to now patients affected by coronavirus are more than 4.28 crore. Davide Gentile *et al*.(2020) The fast growth of SAARS-CoV-2Coronavirus infection in people with the severe acute respiratory syndrome) has triggered a global health emergency from this paper heidentifies possible targets andChloroquine and hydroxychloroquine's method of action against SARS-CoV-2, He employed docking and simulation methodologies. He found that both drugs act against the SARS-CoV- 2 and Interactions, which affect the protein structure's adaptability and influence the functionality of the envelope (E) protein, which is required for the virus's maturation activities. Furthermore, in SARS-CoV-2, chloroquine and hydroxychloroquine impacted the proof reading and capping of viral RNA.[17]

2.8 Anti-tuberculosis activity:

The World Health Organization (WHO) claims that By 2020, an estimated ten million people would have contracted tuberculosis (TB) worldwide. Rajkumar Reddy rajula*et al*.2019 has been discovered A novel class of quinoline-1,2,3-triazole compounds. cognates were designed using the principle of molecular hybridization and Quinoline and 1,2,3-triazole are linked via ether or an amide functional group. because the linker group structure is modified and enhanced the anti-tubercular activityof the compounds When compared to their ether analogues, all of the amide compounds demonstrated better inhibitory action.According tothis research paper compounds 8a., 8b., 8c., 8d., and 8e. are shows substantial anti-tuberculosis action.



8

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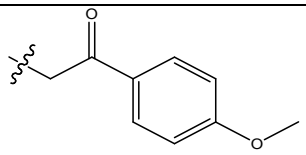
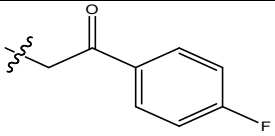
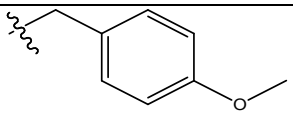
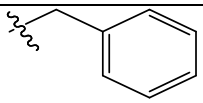
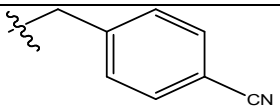
Compounds	R
8a	
8b	
8c	
8d	
8e	

CONCLUSION

According to literature review it was found that quinoline shows various activities such as Antimalarial, anticancer , antibiotic, anti-inflammatory, anti-tubercular activity, anti viral activity among them the new investigation of quinoline is anti SAARS- Cov -2 , in SARS-CoV- 2, chloroquine and hydroxychloroquine impacted the proof reading and capping of viral RNA. And I was also found that it give better antibiotic activity because it is effective against in *vitro* bacterial strains of Pseudomonas pyocyanin, Escheerichiaa colie, Streptococcus faecaaliis, and Stephyllococcus aureeus.

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Conflict of Interest

The authors declare that they have no conflict of interest