EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 4
Issue: 12
223-231
Year: 2017

REVIEW ON SYNTHESIS AND BIOLOGICAL EVALUATION, STRUCTURAL ACTIVITY RELATIONSHIP OF QUINOLINYLCHALCONE CONTAINING PYRAZOLINE DERIVATIVES

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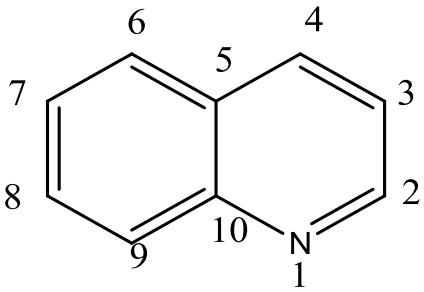
Article Received on 03/10/2017 **Article Revised on 24/10/2017** **Article Accepted on 15/11/2017**

ABSTRACT
Quinolinylchalcone containing pyrazoline derivativtes have wide range of pharmacological activity such as anti cancer, anti viral, anti inflammatory, anti malarial, anti diabetic, anti fungal, anti protozoal etc. the review focus on developed strategies on synthesized compounds and to study substituent and nucleus effect on biological activity.

KEYWORDS: quinolinylchalcone, pyrazolines, structural activity relationship.

INTRODUCTION

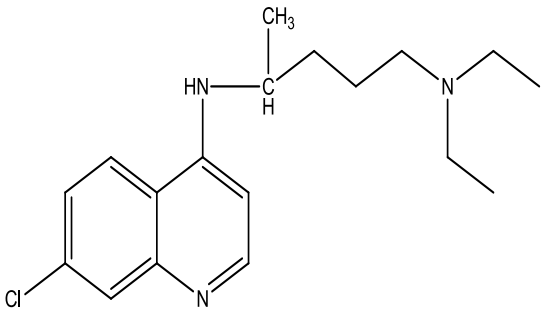
Quinoline (1-azanaphthalene or benzopyridine) is an aromatic nitrogen containing compounds characterized by a double ring structure where the benzene ring is fused to pyridine at two adjacent carbon atoms it is hygroscopic yellowish oily liquid slightly soluble in water, alcohol, ether, carbon disulfide molecular formula is C_9H_7N.

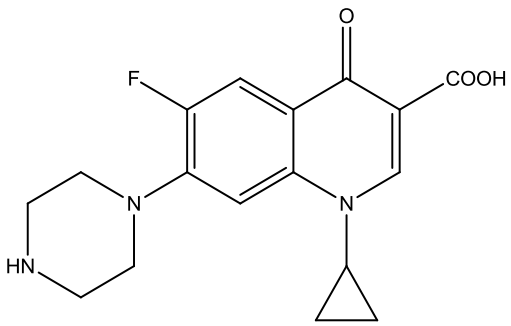


General structure of quinolone

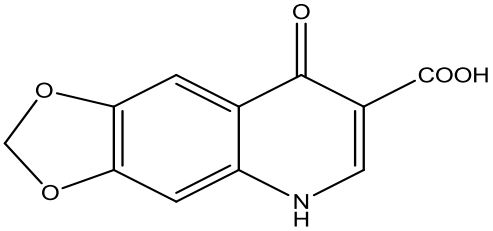
The first compound introduced in the year of 1963 for treating urinary tract infection. They prepared for aniline with acrolein under heated sulphuric acid. Various derivatives can be prepared by strap synthesis using different oxidizing agents. These compounds have wide range of biological activities such as anti malarial, anti cancer, fungicidal, bactericidal, anti amoebic etc.

Some of marketed released drugs are ciprofloxacin norfloxacine



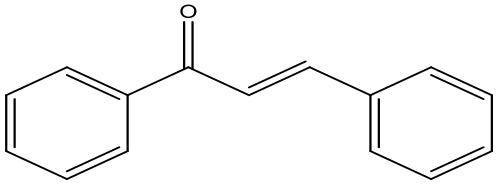


Oxalinic acid

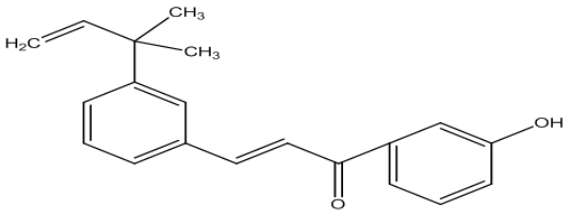


Chalcones were chemically 1, 3- diphenylpro-2-en-1-one/ bezalacetophenone/ benzylidine acetophenone/ phenylacrylphenone. They widely distributed among nature. It is well known intermediate for synthesis of various heterocyclic compounds and reported to exhibit a variety of biological activities such as anti malarial, anti inflammatory, anti viral, anti cancer, anti tubercular, anti hyperglycemic etc.

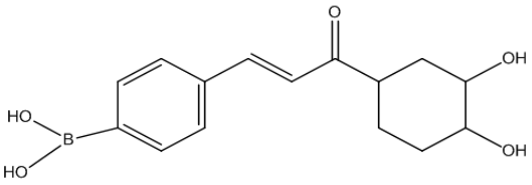
General structure of chalcone



Marketed released chacones.

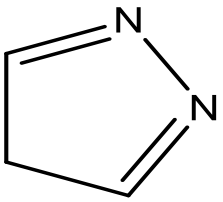


Licochacone



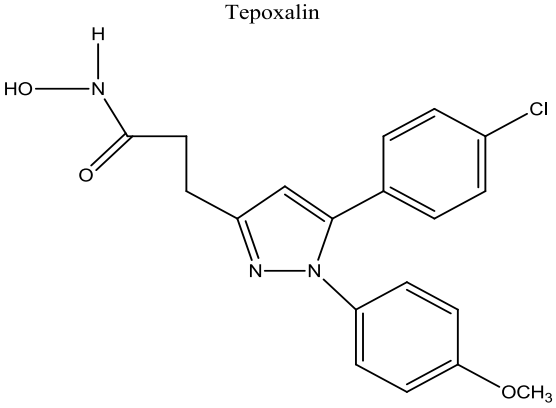
Boric chalcone

Pyrazolines are dihydric derivatives of pyrazole and are well known five member nitrogen containing compound. It has been reported by the action of nucleophile like hydrazine hydrate or phenyl hydrazine by using alcohol as a solvent. Pyrazoline are associated with diverse biological activity such as anti tubercular, anti inflammatory, anti depressant, anti tumor, anti convulsion etc by considering the above facts and increases importance in pharmaceutical and biological field, it was considered of interest to synthesize new chemical entities incorporating the two active pharmacophores in a single molecular frame work and to evaluate their biological activity.
General structure of pyrazole.

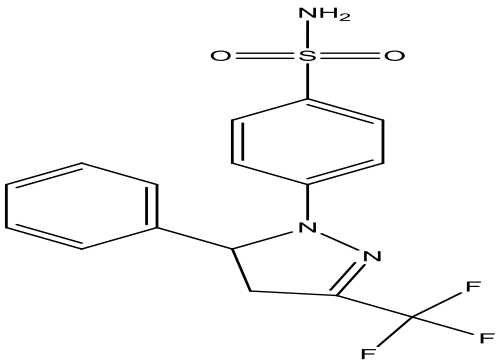


Marketed released pyrazole moiety containing drugs

Tepoxalin



Celecoxib

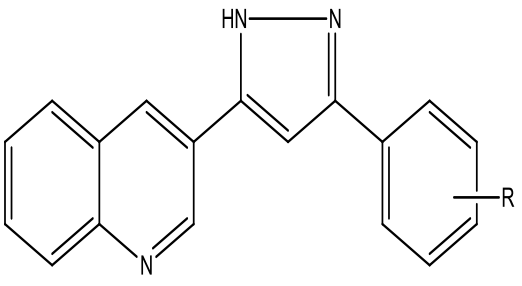


Quinolinylchalcone containing pyrazolines

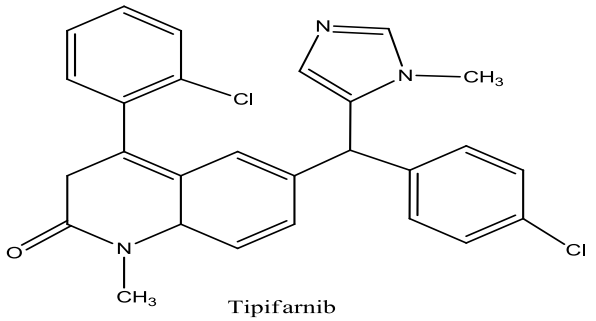
Chalcones are considered as very useful precursors of the preparation of different heterocyclic compounds like flavanoid, quinolines, pyrazolines, pyridines, thiazepines, isoxazoles. The member of quinoline family has wide range of therapeutic uses as chalcone. The substitution of an aryl group of chalcones by a quinoline moiety would enhance the biological activity like anti cancer, anti malarial, anti viral, analgesic, inflammatory etc.

Pyrazolines are five member hetero cyclic compounds with two adjacent nitrogen atoms would prepare for chalcone by the michael addition reaction. It has been reported both naturally occurring and synthetic chalcons and pyrazolines. It possesses a wide range of biological activity such as anti oxidant, anti malarial, anti fungal, analgesic, inflammatory etc.

General structures of aryl substituted chalcone by a quinolinylpyrazoline moiety.



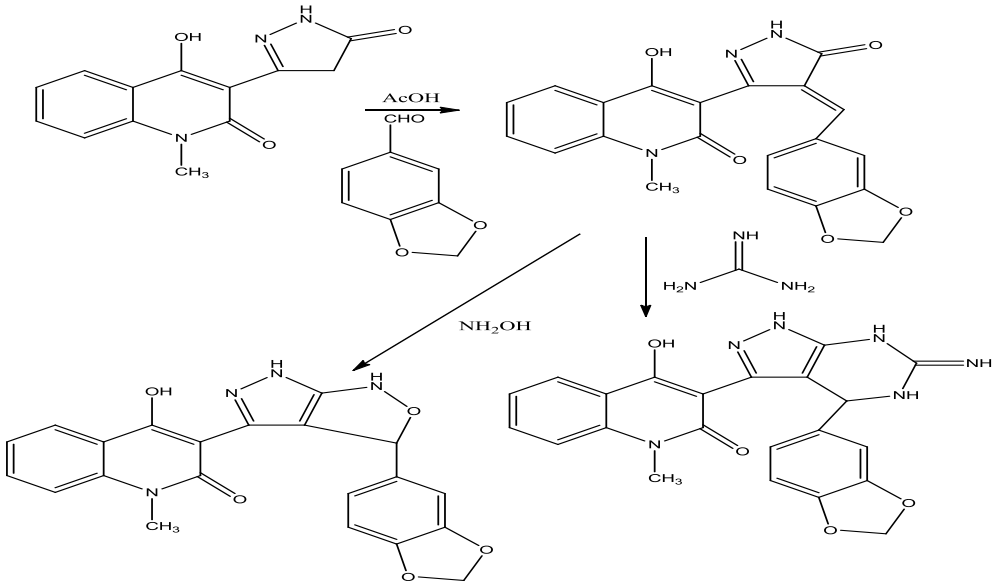
Marketed released quinolinylpyrazole.



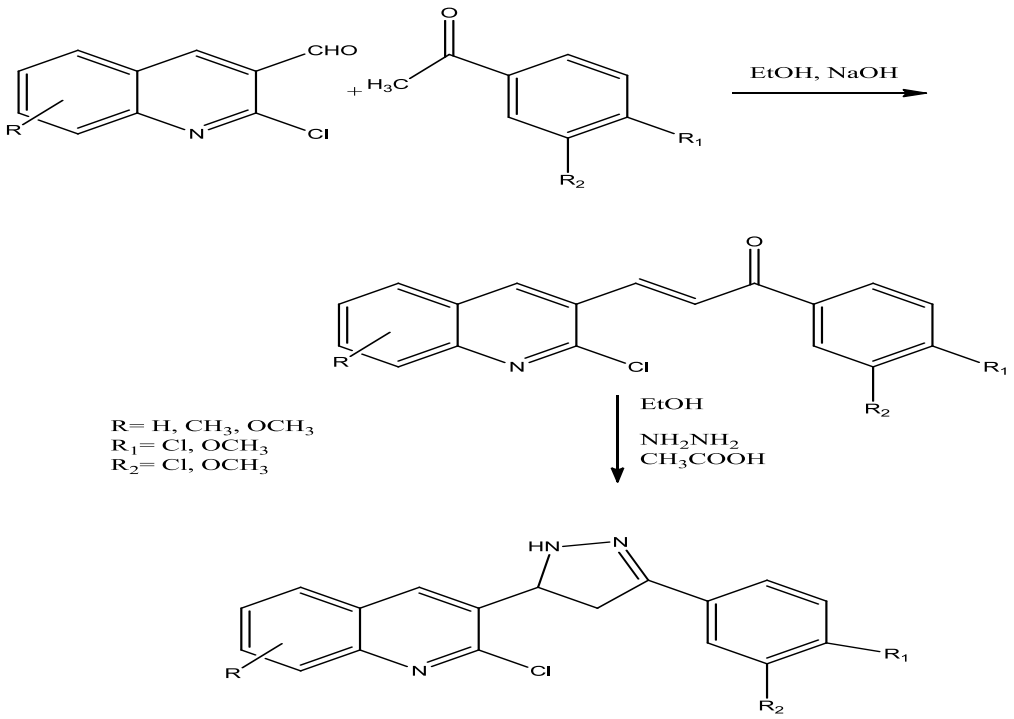
Tipifarnib

Elham S.Otham et al., (2003) synthesis of 3,4 benzo 1,3-dioxyolylmethylene pyrazolylquinoline-2-one derivatives from N-methyl quinolinylpyrazoline-2-one with acetic acid for cyclization then treated with different amino compounds.

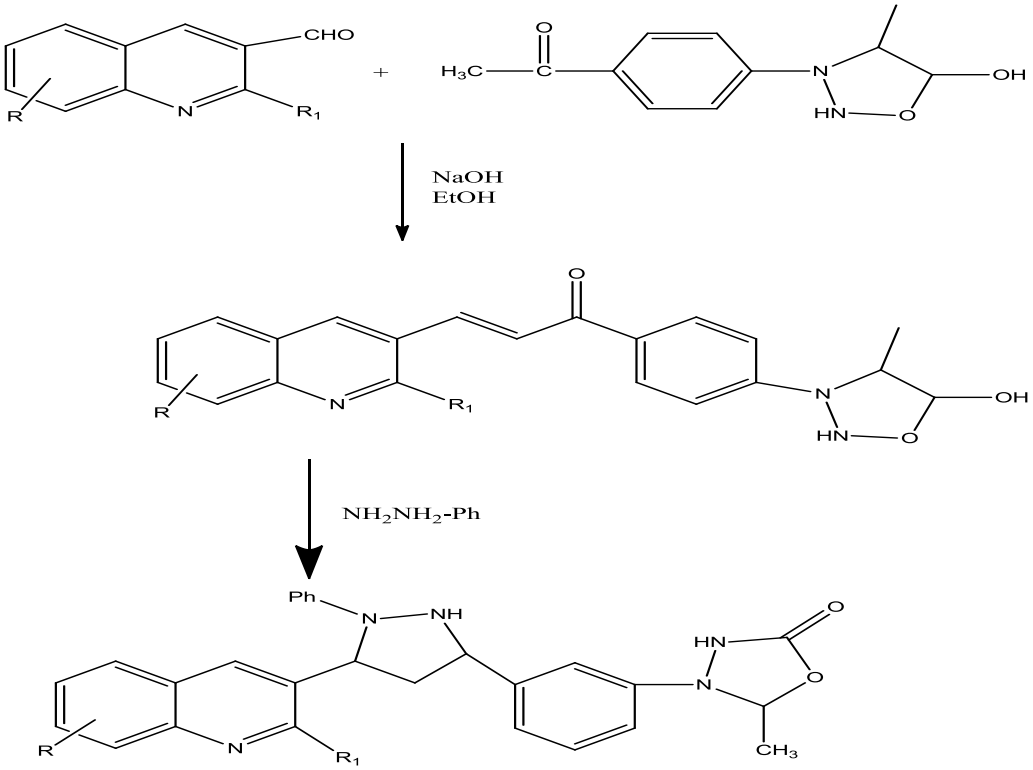
Different schems for synthesis of quinolinylchalcone and pyrazoline derivatives.



Sandhya bawa, suresh kumar et al., (2009) synthesis of 2-chloroquinoline incorporated pyrazoline derivatives from substituted 2-chloroquinoline3-aldehyde with different substituted aromatic ketones in ethanol give quinolinylchalcones again treated with hydrazine in presence of acetic acid, ethanol.

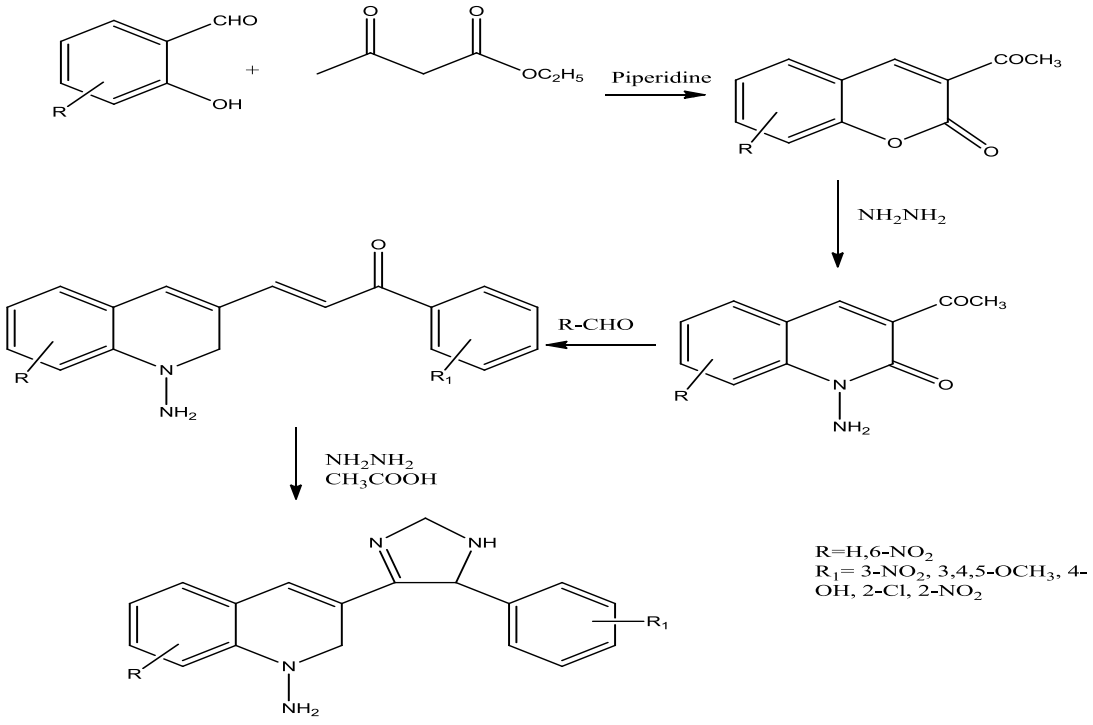


Kumar sanjeev S.Lamani et al., **(**2013) synthesized substituted quinoline based 2-pyrazoline from substituted quinoline 3-aldehyde with acetyl phenyl sydnone in presence of sodium hydroxide.



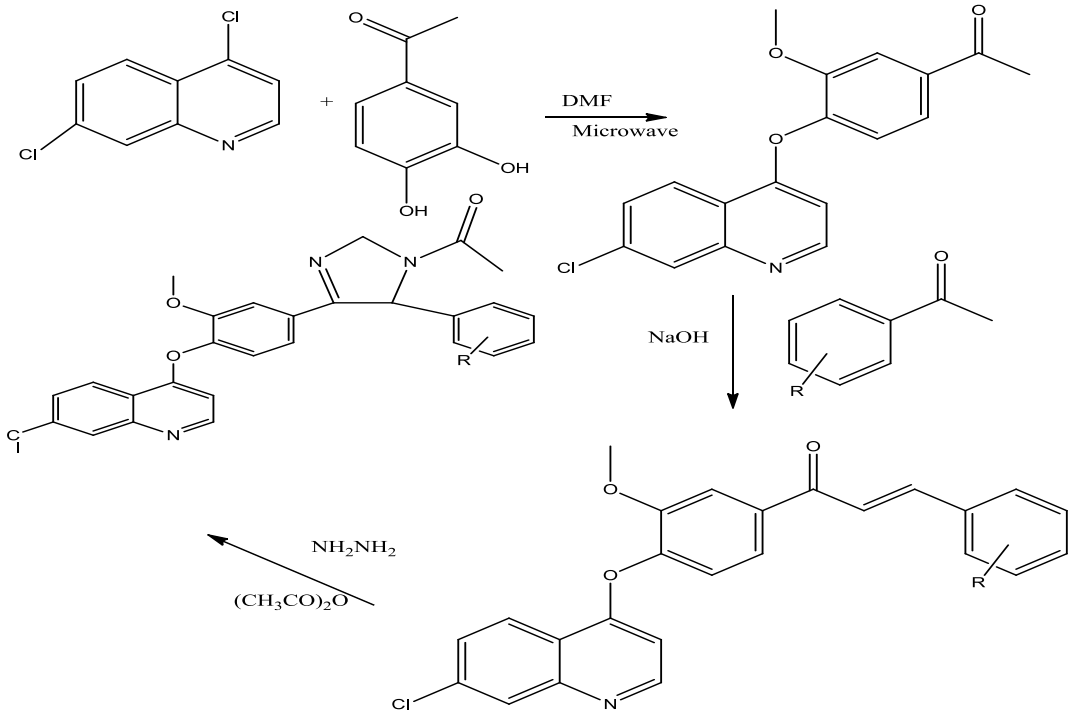
R= Cl, SH, Cl, SH, Cl,SH,Cl, SH
R_1=H,H,OCH_3,OCH_3,OH,OCH_3,NO_2, NO_2.

Jennifer fernandes et al., (2013) synthesis of pyrazoline derivatives derived N-substituted quinolinylchalcones from different substituted salicyaldehyde with ethylacetoacetate in presence of pyridine and hydrazine to form N-substituted quinoline 3-acetyl-2-one treated with different aromatic aldehyde to form N-substituted quinolinylchalcone derived pyrzolines.

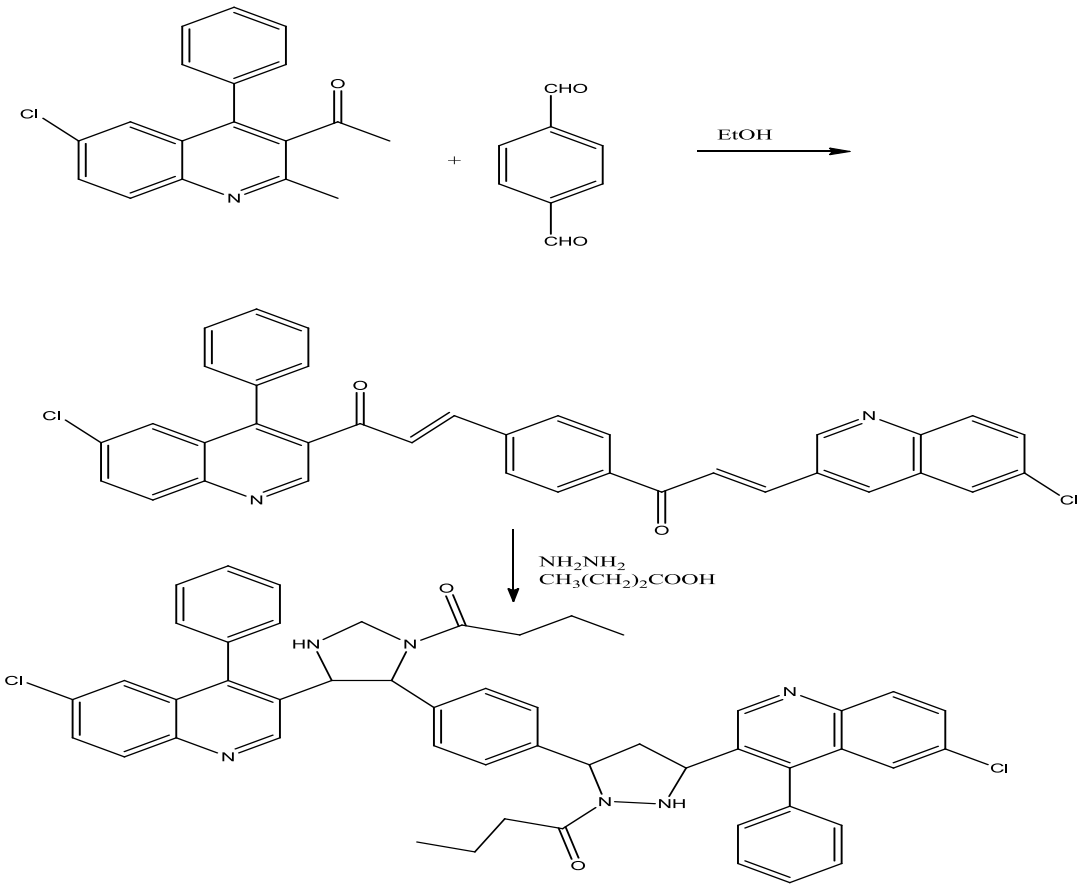


R=H,6-NO_2
R_1= 3-NO_2, 3,4,5-OCH_3, 4-OH, 2-Cl, 2-NO_2

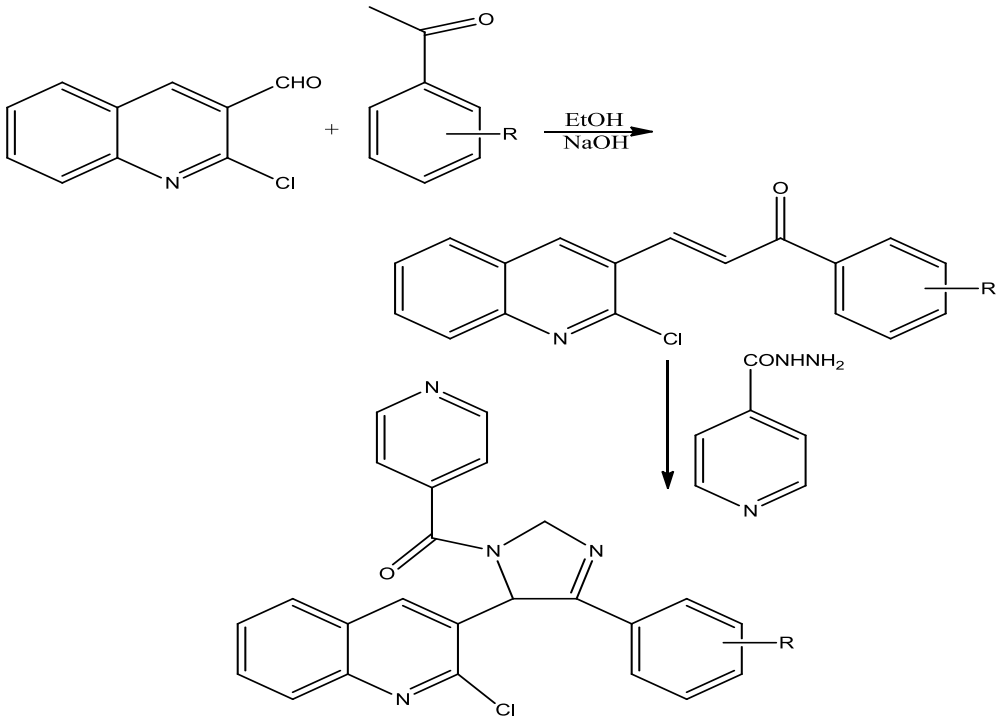
Alba monotony et al., (2014) synthesis of 2-pyrazoline derivatives bearing the 4-aryl oxy-7-chloroquinoline from dichloroquinoline with aromatic aldehyde to form quinolinylchalcones then treated with hydrazine in ethanol and acetic anhydride with pyridine to gives 4-aryl oxy 7-chloroquinolinyl derivative of pyrazoline.



Allaona kedjadja et al., (2015) Synthesized aromatic quinolinyl dihydro pyrazolines. 2 molecules of aromaticquinoline treated terataldehyde in presence of hydrazine and butanoic acid.

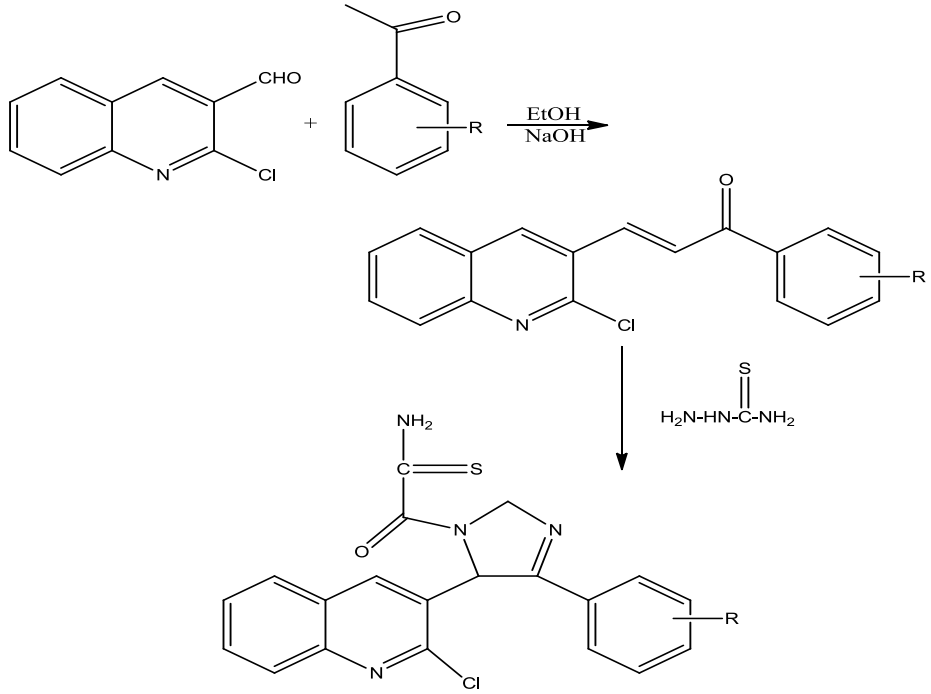


Nisheeth etal., (2016) synthesis of 2-chloroquinolinyl 4,5-dihydro pyrazol-1-yl-pyridine methanone from 2-chloroquinoline3-aldehyde with different aromatic ketones in ethanol give quinolinylchalcones again treated with isoniazide.



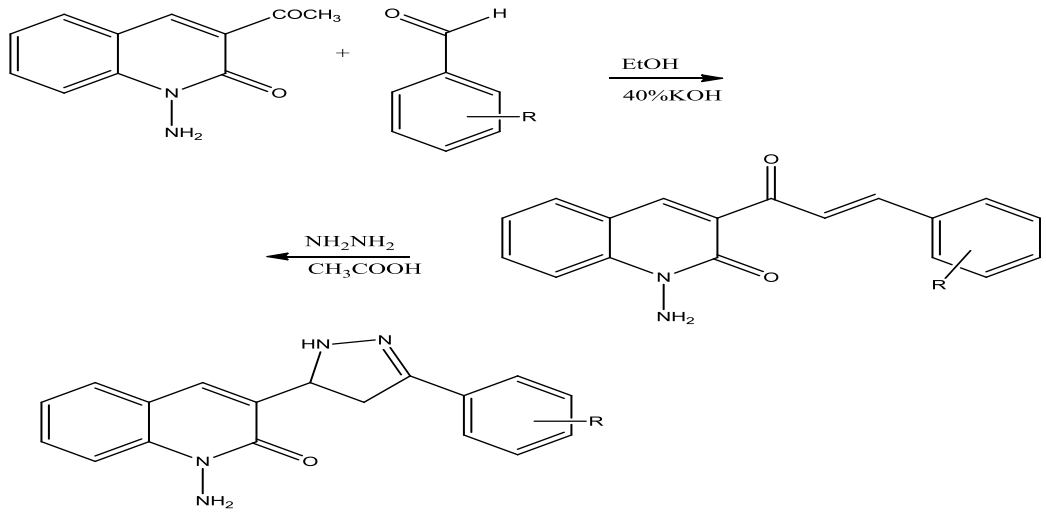
R= H, 2-CH_3, 2-OCH_3, 4-CH_3, 4-OCH_3, 2-OH, 2-Cl

Hallikeri etal., (2016) synthesis of 2-chloroquinolinyl-3-phenyl4,5-dihydropyrazoline-1-carbothioamide from 2-chloroquinoline3-aldehyde with different aromatic ketones in ethanol give quinolinylchalcones again treated with hydrazine thioamide.



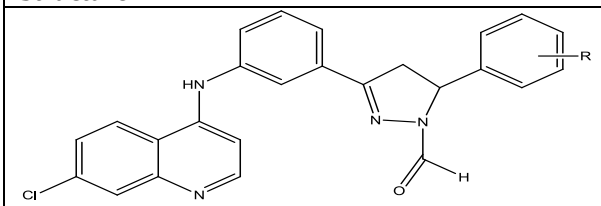
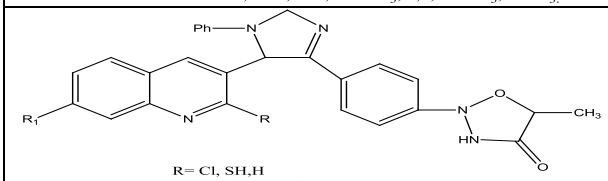
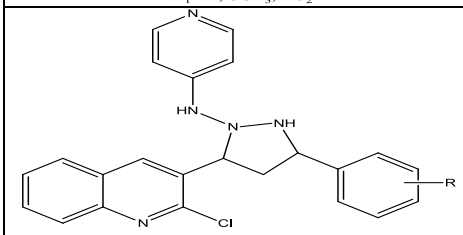
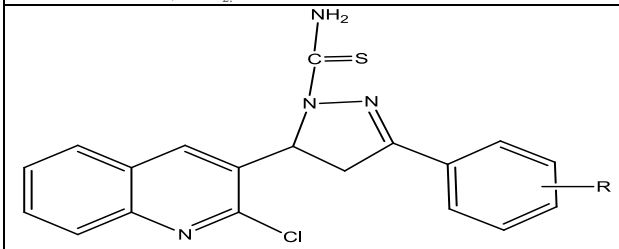
R= H, 2-CH_3, 2-OCH_3, 4-CH_3, 4-OCH_3, 2-OH, 2-Cl,3-OCH_3, 3-Br

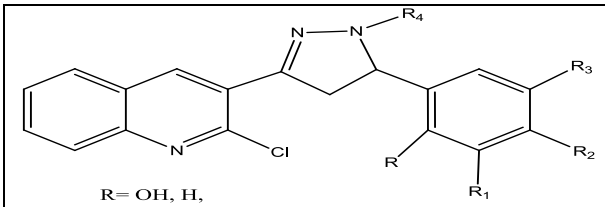
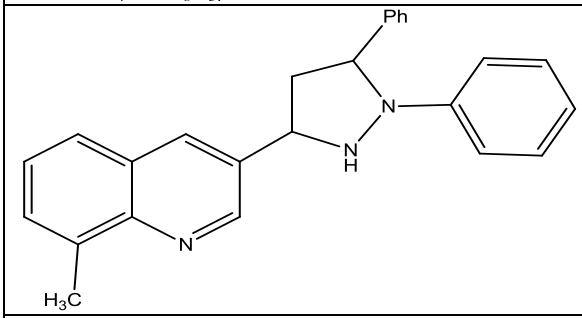
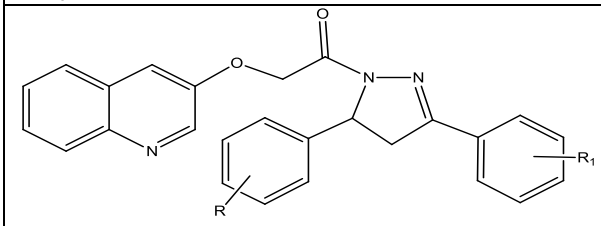
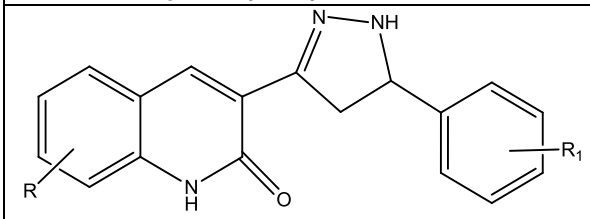
Abhishek kumar et al., (2016) synthesis of novel pyrazoline incorporated quinolones from 1-amino quinoline 3-acetyl-2-one reacted with different substituted aromatic aldehyde in etanol to from N-substituted quinolinylchalcones again treated with hydrazine in acetic acid.



R= 3-CH_3, 3,4,5-OCH_3, 6-NO_2.

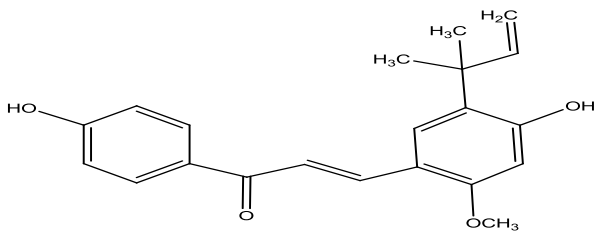
Biological evaluation of quinolinylpyrazolines.

Structure	Biological activity	Author name
 R= 4-Br, 4-Cl, 4-H, 4-OCH_3, 3,4,5-OCH_3, 4-CH_3.	Anti tumor activity	*Alba Montoya et al.*
 R= Cl, SH,H R_1= H, OCH_3, NO_2	Anti bacterial, anti fungal activity	*Kumar Sanjeev S.Lamani et al.*
 R= H, 2-CH_3, 4-CH_3, 2-Cl, 4-Cl, 4-F, 4-Br, 2-OCH_3, 2-OH, 3-OH 4-OH, 4-NO_2.	Anti microbial activity	*Nisheeth C.Desari et al.*
 R= H,4-OCH_3, 4-Br, 4-NO_2, 4-NH_2, 4-Cl, 3-Br, 3-OCH_3, 4-CH_3.	Anti microbial activity	*C.S Hallikeri Naveen V et al.*

 R= OH, H, R_1= I, Br, Cl R_2= OH, H R_3= I, Cl, CH_3, Br R_4=H, C_6H_5.	Anti microbial activity	*Shyam S. Mokle et al.*
	Anti mycobacterial activity	*Ozdemir A. Asim ZG, et al.*
 R= 4-Br, 4-Cl, h R_1= 4-OCH_3, 4-CH_3, 2-Cl, 3-Cl.	Anti amoebic activity	*F.Hayat et al.*
 R= H, 6-OCH_3 R_1= 3-NO_2, 3,4,5-OCH_3, 4-OH, 2- Cl, 2-NO_2	Anti inflammatory activity	*Jennifer Fernandes et al.*

Structural activity relationship of quinolinylpyrazolines

The anti malarial activity of chalcones was first noted licochalcone A1 is a natural product isolated from Chinese liquorice roots it reported to potent anti malarial agent.

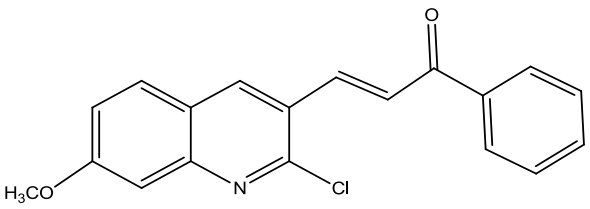


Licochalcone A1

The good effects were exerted by alkoxychalcone with polar B ring in a particular electron with drawing group incorporated in to quinoline moiety.

Quinolinylbenzocyclochalcone inhibits β-hematin formation and hydrolysis of haemoglobin invitro in rodent plasmodium bergei. The inhibition of hematin was minimal when introducing hydrogen or methoxy group at 8th position of quinoline ring.

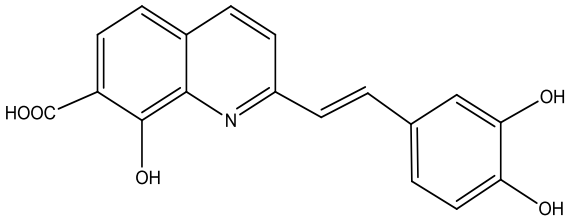
N at 1st position assists as a weak base causes drug accumulation via p^{H} trapping. Quinoline group is heme complex group, introduce Cl at 7th positions inhibit β-hematin formation.



8-hydroxy quinoline is inactive by the addition of C7 Carboxyl group does not affect the activity. It replaced to introduce electron withdrawing atoms such as nitro group suppressed the activity introduces methyl/ carboxyl group of C2 impairs orientation towards the nitrogen atom in which polar group such as carboxyl group at C7 position improve the binding affinity towards integrase enzyme.

Phenolic hydroxyl group at C8 inhibited to integrase activity. While it replaced with nitro/ carboxyl of C8 positions of quinoline decreases the activity. Amino group was fixed at C8 indicate that a simple hydrogen bonds donar residue is inefficient in promoting inhibition.

The addition of nitrile at C7 in quinoline shows less anti integrase activity. Carboxyl group at C7 replaced with carbomethyl group completely devoid of biological activity.



The free carboxyl group greatly improves the integrase inhibition. At C2 position introduce subunit of dihydroxyphenylethylene shows equal potent as that of carboxyl at C7 position.

CONCLUSION

The literature surveys to gives information about recently no of conventional methods used to synthesized different substituted quinolinylchalcone containing pyrazolines effect on biological activity. To study the structural activity relationship introducing different substituent on quinoline moiety effect the potency and binding affinity with the targeted molecule. From the different synthetic strategies of quinolinylpyrazoline derivatives it also synthesized from different substituted benzophenones and different substituted aromatic aldehydes are used to synthesis different disubstituted quinolinylchalcones derivatives then it treated with hydrazine hydrochloride to form quinolinylpyrazolines derivatives it may be have anti cancer, anti diabetic, anti oxidant, anti microbial activity.

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