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A REVIEW ON NEWLY SYNTHESIZE QUINOLINE BASED COMPOUNDS & ITS PHARMACOLOGICAL ACTIVITY

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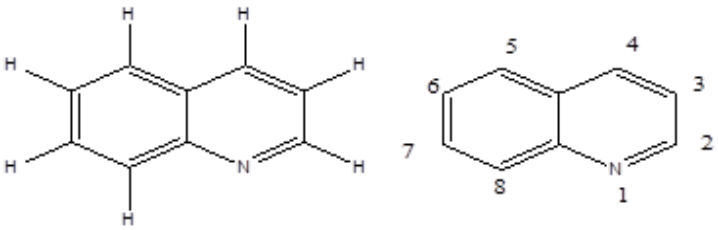
ABSTRACT

Quinoline and its fused heterocyclic derivatives evaluated for any pharmacological activities provided important role in medicinal chemistry and new drug development. There for every researcher have synthesized new derivatives and evaluated their's pharmacological activities. The present review provided an in deepness study on Quinoline its biological activities covering, Insecticidal activity, antibacterial agents/DNA gyrase inhibitors, anti-diabetic agent, anticancer agent, antitumor drug, antifungal, antibacterial antiprotozoal agents, α-Amylase Inhibitory activity, anticonvulsant activity, anti-inflammatory activity, antimicrobial activity.

KEYWORDS: Quinoline, Insecticidal activity, antibacterial agent, anti-diabetic agent, anticancer agent.

INTRODUCTION

Quinoline



Quinoline nucleus is a fused aromatic ring systems also known as benzo(b)pyridine. Quinoline shows aromatic properties because the resulting molecular orbital satisfies the

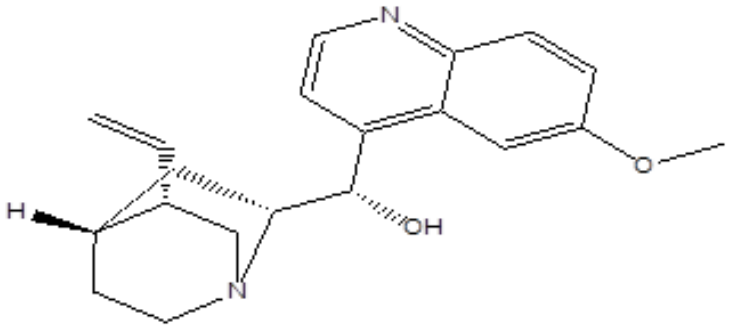
Huckles' s rule (4n + 2 rule). Quinoline is a heterocyclic ring compound and ring contain 9 carbon atom and one nitrogen atom. All quinoline ring are sp_2 hybridized.

Quinoline nucleus is very important pharmacophore in medicinal chemistry, since quinolone derivative are provided the pharmacological activity such as antimalarial, anti-inflammatory, anti-hypertensive, anti-diabetic, anti-asthamatic, anticonvelsent and tyrosine kinase inhibiting agents.

Sources of quinolone included petroleum, wood preservation, coal processing, production and uses abilities and shale oil. Quinoline has also sbeen detected in coke oven tars and tobacco smoke.

Quinoline are less reactive toward electrophilic substitution than benzene because of the electronegative nitrogen atom that withdraw electrons from the ring.

First quinolone antimalarial drug quinine was alkaloids take out from cinchona tree. The cinchona tree is title after the countess of chinchon, who according to myth was treated of malaria in 1630 by a powder made from its bark.



quinine

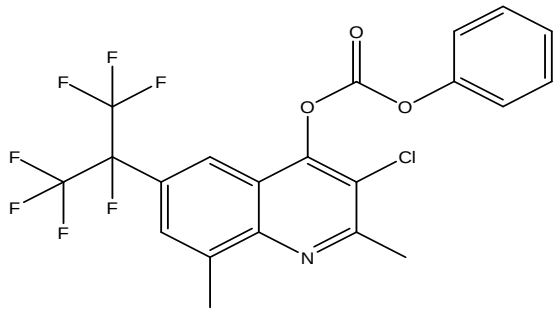
Review of Literature

The survey of literature has discovered numerous therapeutic uses of quinoline and its derivatives. The most effective pharmacological action provided under that quinoline derivatives can be classified are:

1. Insecticidal Activity

Xing-Hai L. et al 2019 have synthesized a new series of 6-perfluoropropanyl quinoline derivatives (4a-4o) were prepared from1,1,1,2, 3,3,3-heptafluoro-2-iodopropane and 2-methyl aniline and using *combes* method for cyclization. Synthesized compound were tested

for insecticidal activity against *Aphis craccivora* by *Finneys method* and compound 4e acquired good insecticidal activity against *M. separata* and *P. xylostella*, and shows 30 % and 60 % inhibitory at 20mg/L and shows 100 % repressive activity against *L. pests* by 500 and 100mg/L. The structure of new synthesized 6-perfluoropropanyl quinoline derivative are characterized by ^{1}H-NMR, MS, and elemental analysis.

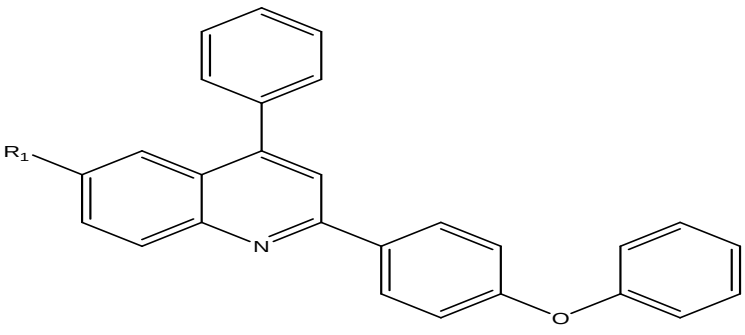


3- chloro-2,8- dimethyl- 6 -(perfluoropropan-2-yl)quinolin- 4-yl phenyl carbonate

4e

2. DNA gyrase inhibitors/ Antibacterial agents

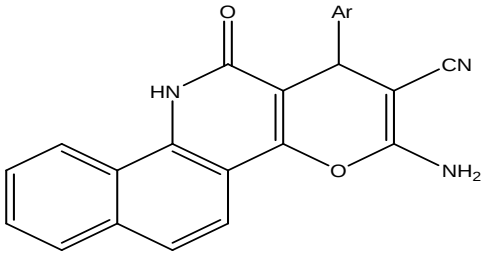
A new series of 6- substituted- 2-(3 -phenoxyphenyl) -4-phenylquinolines (4a-h) have been synthesized by refluxing consistent anilines, 1-ethynylbenzen and 3-phenoxybenzaldehyde in nitro methane solution / iodine and cuprous oxide, by Sivakumar A. et al (2017). New synthesized series of 6-substituted-2-(3-phenoxyphenyl)-4-phenylquinolines derivatives (4a-h) in 4c(IC50 0.357 µg/mL), 4d(IC50 0.822±0.28 µM; relative inhibition 72%), 4e (IC50 0.694±0.21 µM; relative inhibition 74 %), and 4h (IC50 0.702±0.12 µM; relative inhibition 73%) were found most humming anti-bacterial activity found agaist Staphylococcus, the gram^{+ve} bacterium and 4a, 4b, 4c, 4d, 4e, 4f, 4g, 4h compound inhibition of S. aureus DNA gyrase.

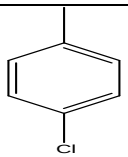


Compound	R
4a	Cl
4b	Br
4c	F
4d	CN
4e	OH
4f	O-CH_3
4g	CH_3 (9 position), CH_3(8 position)
4h	Cl (8,10 position), OH-R position

3. Anti-diabetic agent

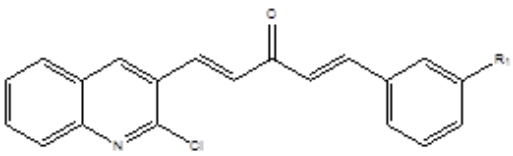
Larijani B. et al 2018 have synthesized a novel series of dihydropyrano[3,2-c] quinoline derivatives 6a -q were synthesized and found active against S.cerevisiae α-glucosidase enzyme in vitro by using Lineweaver-Burk plots method and prepared compound 6a,6d,6e,6g,and 6l were tested for α-glucosidase inhibitory activity and evaluated for toxicity. In this series 6e shows most potent activity.



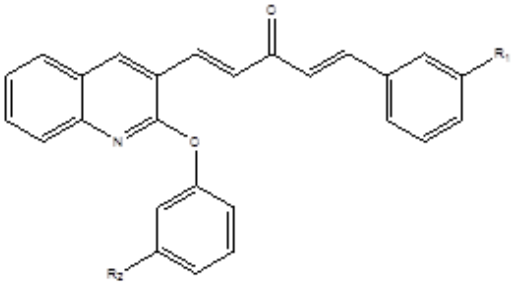
Compound	Ar
6e	

4. Anticancer agent

A new series of quinoline derivatives (6a-6d) and (9a-9p) have been synthesized by the using Claisen-Schmidt condensation and Vilsmeier-Haack reaction method, by Ahmed Kamal etal 2018. In a new synthesized series (6a-d) and (9a -p) series were screend in vitro for their cytotoxic activity to wards various tumor cell line. In this series most active compound 6c shows capable cytotoxicity against PC-3 (IC_{50} of 3.12±0.11μM), NCI-H460, DU-145 and 4TIcell lines and 6d screened compound most active and exhibited significant activity analogue.



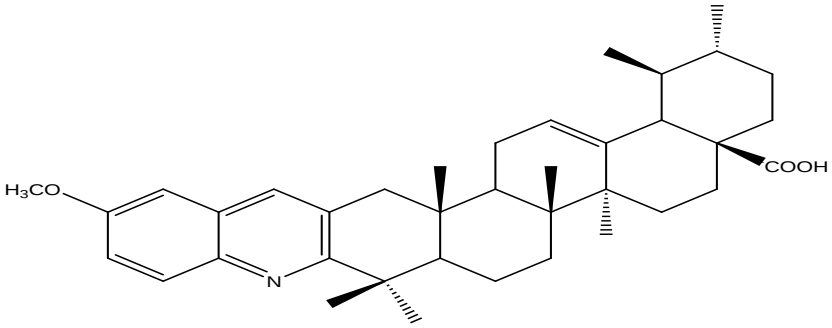
6c: R_1= 2,4,5-triOCH_3



9d: R_1=2,4,5-triOCH_3, R_2=H

4.2:

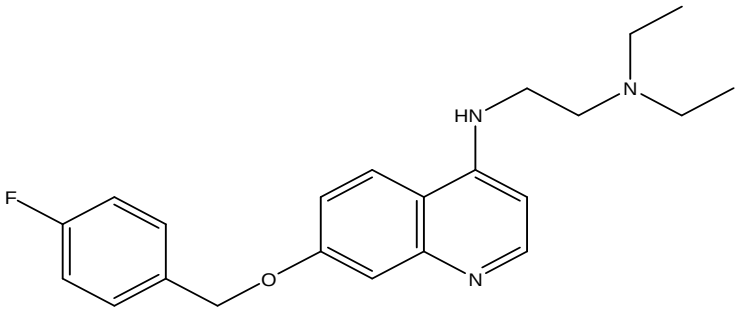
A new sequences of quinoline derivative of ursolic acid have been synthesized by Wen G. et al 2017. New series of quinolione derivative of ursolic acid have been synthesized compound (3a-d) (4a-l) (5a-l) but in a compound 3a-d displayed significant antitumor activity counter to three cancer cell lines (MDA-MB-231, SMMC-7721 and Hela). Compound 3b was especially most potent derivative.



3b

5. Antitumor drug

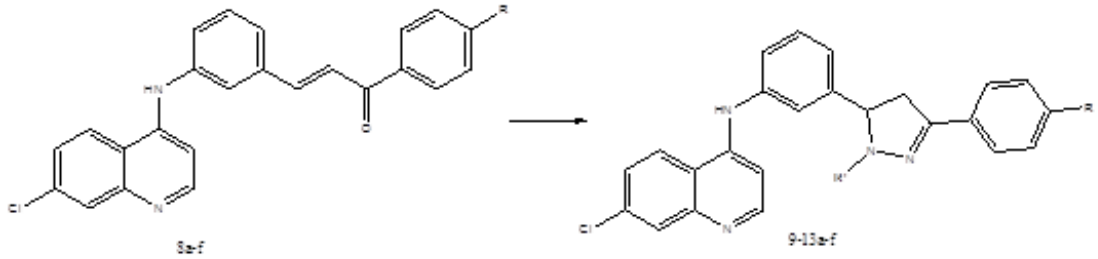
Cao R. etal 2018 have synthesized a new series of new quinoline derivative, 7- (4 -fluorobenzyloxy)- N-(2-(dimethylamino)-ethyl)quinolin -4-amine (10g)) were synthesized, designed and evaluated as potential anti-tumor agents. All synthesized compounds displayed potent anti-proliferative activity, and (10g) was displayed most potent anti-proliferative compound against human tumor cell lines with an IC_{50} values of less then 1.0 µM.



10g

6. Anticancer, Antifungal, Antibacterial and Antiprotozoal agents

Insuasty Braulio et al 2017 have synthesized a new sequences of N-substituted 2-pyrazolines derivatives were synthesized by cyclo-condensation reaction. A new series of compound have been shows the anti-bacterial activity counter to some type and multidrug resistant gram positive and gram negative bacteria and some additional compound showed anti-fungal and anti-parasitic activity. Although these compounds displayed mild activity against Candida albicans, chalcones 8a and 8e displayed high activity against Cryptococcus neoformans with MIC_{50}= 7.8µg/ml and 11b showed most activity against anti-plasmodium falciparum with EC_{50}=5.54µg/ml and 10a showed highly activity against trypanosome cruzi with EC_{50}=0.70µg/ml. Chalcone 8a has displayed good action against leishmania panamensis amastigotes with EC_{50}=0.79µg/ml.



8a-f 9-13a-f

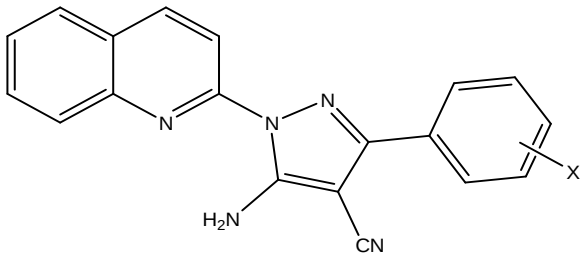
R'= /-$COCH_3$ -CHO -C_6H_5 -4-Cl-C_6H_4 -3,5-diCl-C_6H_3

9a-f 10a-f 11a-f 12a-f 13a-f

8-13	R	Anticancer activity	Antifungal activity	Antibacterial activity	Antiprotozoal activity
a	Cl	**8c** GI_{50} 0.49µM	**8a** MIC_{50} 7.8µg/ml	**9d** MIC 31.25µg/ml	**11b** EC_{50} 5.54µg/ml
b	Br	**8d** GI_{50} 0.31µM	**8e** MIC_{50} 7.8µg/ml		**10a** EC_{50} 0.70µg/ml
c	OCH_3	**10a** GI_{50} 0.28µM			**8a** EC_{50} 0.79µg/ml
d	3,4,5-$(OCH_3)_3$	**10c** GI_{50} 0.37µM			
e	CH_3				
f	H				

7. Antifungal and Antibacterial activity

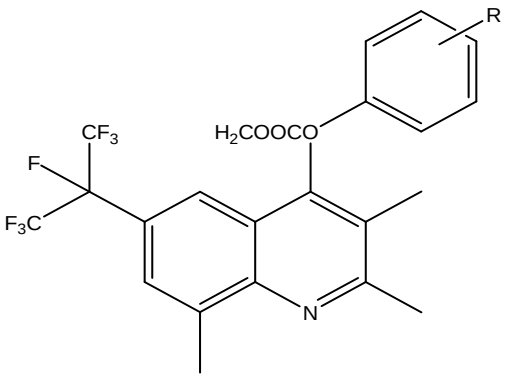
Ammar Y. A. etal 2017 have synthesized a three new quinoline derivatives series were synthesized by Clasien-Schmidt condensation and cyclocondensation, The synthesized compound displayed potent antifungal and antibacterial activities against the tested strains of fungi and bacteria by using Agar-diffusion method. In this series 13b displayed best result when compared with the reference drugs as exposed from their MIC values (0.12- 0.98 µg /ml) and 13 b compound inhibiting the growth of S.flexneri (MIC 0.12 µg/ml), A.clavactus, C.albicans, P.vulgaris, S.epidermidis, A.fumigatus. The structure have been characterized by NMR, IR, mass spectra.



13b X=2,4-Cl_2

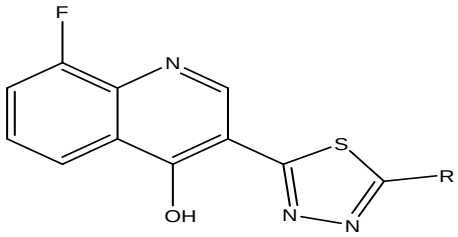
8. Fungicidal Activity

A new synthesized series of quinoline derivatives containing 1,1,1,2,3,3,3 - heptafluoropropan- 2 -yl moiety have been synthesized by Liu X.-H. et al (2017). A new synthesized series have been showed fungicidal in vivo activities against rice blast even at 10m /L by the using of host plates method. In a new synthesized series Benzyl(2,3, 8 - trimethyl-6- (perfluoropropan-2 -yl)quinoline-4-yl) carbonate showed most potent fungicidal activity.



9. α-Amylase Inhibitory Activity

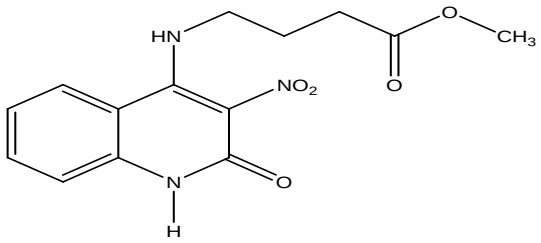
A new series of Thiadiazole Quinoline derivative have been synthesized by Thio-hydrazide smoked with aryl aldehydes to form cyclized adducts or new series of Thiadiazol Quinoline derivatives, by Muhammad T. et.al 2017. A new series of derivatives (1-30) were synthesized and screend for α- amylase inhibitory action provided mutable degree of α-amylase inhibition with IC_{50}values. The new synthesized thiadiazole quinoline analoges structure have been charecterized by ^{1}HNMR, EI-MS and different spectroscopic techniques.



Thiadiazole quinoline derivatives (1-30)

10. Anticonvulsant Activity

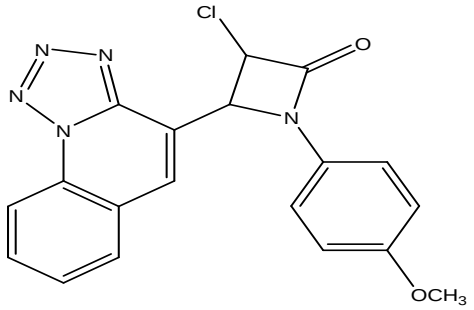
Novel thiocumarins and quinoline-2-ones have been synthesized by G.C.Mokrov et al 2019. This novel series were synthesized and screened for anticonvulsant activity. A novel series 2a-b,3a-b in a methyl ester 3 a had the most potent anticonvulsant activity in mouse tests at a dosage of 12.5 mg /kg(i.p). Synthesized compounds with such activity were discovered in carazole antagonism and maximal electroshock (MES) test.



3a

11. Anti-inflammatory activity

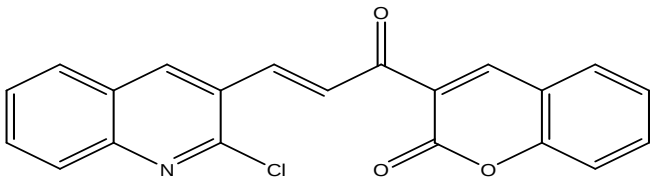
Gupta S. k. and Mishra A. 2016 have synthesized a sequences of Quinoline derivatives (6a-i) bearing Azetidinones scaffols were synthesized by the Vilsmeier-Haack reagent. A novel series of 6a-I were evaluated for their anti-inflammatory and analgesic activities by using Eddy's hot plate method and carrageenan induced rat paw model respectively. In this series 6b displayed 60.32% inhibition for anti-inflammatory activity.



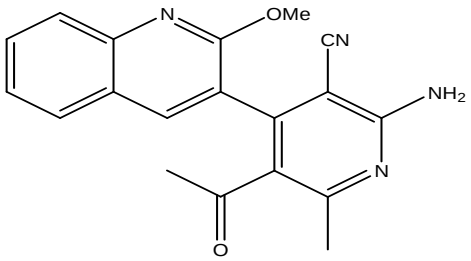
3-chloro-1-(4-methoxyphenyl)-4-(tetrazolo[1,5-*a*]quinolin-4-yl)azetidin-2-one

12. Antimicrobial Activity

Hamama w. S. etal 2016 have synthesized a novel sequences of Quinoline derivatives were synthesized and evaluated for anti-microbial activity. New series of quinoline derivatives were evaluated for their invitro anti-bacterial activity counter to Grampositive bacteria (MTCC-433) and gram-negative bacteria (MTCC-433) and fungal using conventional both Agar- diffusion method. In the series compound 3 and 6 displyed most potent activity.



3-((*E*)-3-(2-chloroquinolin-3-yl)acryloyl)-2*H*-chromen-2-one



5-acetyl-2-amino-4-(2-methoxyquinolin-3-yl)-6-methylpyridine-3-carbonitrile

CONCLUSION

The survey of literature has discovered numerous therapeutic uses of quinoline and its derivatives. The most effective pharmacological action provided under that quinoline derivatives can be classified are, Insecticidal activity antibacterial agents/DNA gyrase inhibitors anti-diabetic agent, anticancer agent, antitumor drug, antifungal, antibacterial antiprotozoal agents, α-Amylase Inhibitory activity, anticonvulsant activity, anti-inflammatory activity, antimicrobial activity. Every researcher have synthesized new derivatives series and provided different pharmacological activity.

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REFERENCES

1. Cheng l., Cai P-P, Zhang R-R, (Synthesis and insecticidal activity of new Quinoline derivatives containing Perfluoropropanyl moiety), Jornal of Heterocyclic Chem., 2019; 00,00.
2. Alagumuthu M., Arumugam S., (Molecular docking, discovery, synthesis, and pharmacological properties of new 6substituted-2 -(3-phenoxyphenyl)-4-phenyl quinoline derivatives; an approach to developing potent DNA gyrase inhibitors/ antibacterial agents), Medicinal Chemistry, 2017; 79: 389-397.
3. Mahdavi M., Nikookar H, Larijani, (Design, synthesis and in vitro α-glucosidase inhibition of novel dihydropyrano[3,2-c]quinoline derivatives as potential anti-diabetic agents) Bioorganic Chemistry, 2018; 77: 280-286.

4. Kamal A., Sri Ramya P.V., Guntuku L, (Curcumin inspired 2-phenoxy/chloro quinoline analougues: Synthesis and biological evaluation as potential anticancer agentes) Bioorganic and Medicinal Chemistry, 2018; 28: 892-898.
5. Cao R, Du R, Qiu L, (Design, synthesis, structure-activity relationships and mechanism of action of new quinoline derivatives as potential antitumor agents) European Journal of Medicinal Chemistry, 2018; 223-5234.
6. Insuasty B., Abonia R., Svetaz L, (Synthesis of novel quinoline – based 4,5-dihydro-1H – pyrazoles as potential anticancer, antifungal, antibacterial and antiprotozoal agents), European Journal of Medicinal Chemistry, 2017; 223-5234.
7. Ammar Y. A., Shehry M.F.El, Shedid S.A, (Quinoline derivatives bearing pyrazole moiety: Synthesis and biological evaluation as possible antibacterial and antifungal agents), 2017; 143-1473.
8. Liu X.-H., Huang H-Y, Tan C.-X.,(Synthesis and In Vivo Fungicidal Activity of Some New Quinoline Derivatives against Rice Blast), 2017; Hangzhou 310023.
9. Taha M., Khan F., Ullah H., (Synthesis and study of the α-Amylase inhibitory potential of Thiadiazole Quinoline Derivatives), 2017; 74: 179-186.
10. Gu W., Chen H, Tao X-B, (Design, synthesis and in vitro anticancer activity of novel quinoline and oxadiazole derivatives of ursolic acid) Bioorganic & Medicinal Chemistry Letters, 2017; S0960-894X(17): 30730-8.
11. Mokrov G.V., (Synthesis and Anticonvulsant activity of 4- Amino-3-Nitro-1-Thiocoumarins and 4-Amino-3-Nitroquinoline-2-Ones), 2019; 53: 3-9.
12. Gupta S.K, Mishra A "Synthesis, Characterization & Screening for Anti-Inflammatory &Analgesic activity of Quinoline Derivatives Bearing Azetidinones Scaffolds" Bentham Science publishers, 2016; 15: 000-0000.
13. Hamama W. S, "A Convenient Synthesis, Antimicrobial Evaluation and Molecular Modeling of Some Novel Quinoline Derivatives" 224-231.