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SYNTHESIS OF DIFFERENT QUINOLINE DERIVATIVES BY MICROWAVE IRRADIATION METHOD

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ABSTRACT

Quinoline nucleus has gathered an immense attention among chemists as well as biologists as it is one of the key building elements for many naturally occurring compounds like quinoline alkaloids, therapeutics and synthetic analogues with very important biological activities such as antimalarial, antiasthmatic, antidiabetic, antibacterial, antiviral, anti-inflammatory, immunosuppressive, anti-breast cancer and anti-proliferative activities. As these quinoline derivatives as many pharmacological activities, we was planned for the synthesis the compounds by conventional method as well as microwave irradiation method, characterized quinazoline derivatives and evaluated for the biological activity.

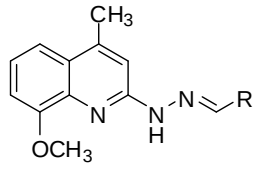
INTRODUCTION:

Quinoline ring is endowed with various activities, such as antituberculosis[1], antimalarial[2], anti-inflammatory[3], anticancer[4], antibiotic[5], antihypertensive[6], tyrokinase inhibiting agents[7]and anti-HIV[8]. Hydrazones are active pharmacophores which posseses an azomethine —NHN=CH— proton constituting an important class of compounds for new drug development. They form a significant class of compounds in medicinal and pharmaceutical chemistry with several biological applications that include antibacterial[9], antifungal[10]and anti-tumor activities[11].

Review of quinoline derivatives: Quinoline nucleus has gathered an immense attention among chemists as well as biologists as it is one of the key building elements for many naturally occurring compounds like quinoline alkaloids, therapeutics and synthetic analogues with very important biological activities such as antimalarial, antiasthmatic, antidiabetic, antibacterial, antiviral, anti-inflammatory, immunosuppressive, anti-breast cancer and anti-proliferative activities.

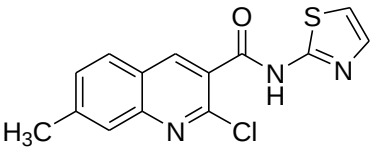
Antimicrobial agents:

S. Singh et al[12] have reported a series of 8-methoxy-4-methyl-2-hydrazinoquinoline Sciff's bases **(7).** These are prepared from 8-methoxy-4-methyl-2-chloroquinoline and 8-methoxy-4-methyl-quinoline-2-ol on reaction with phosphorous oxychloride. The synthesized compounds are evaluated for their *in vitro* antibacterial activity.



R = -C_6H_5 , 4- OCH_3 C_6H_4, 2-Cl C_6H_4**(7)**

Sayed et al[13] have reported several quinoline derivatives which bear a simple alkyl (or) alkoxy group in the 7-position while a free carboxylic or carboxamide function is located in the 3-position. The location of a methoxy group in the 7-position of the quinoline nucleus enhanced the antibacterial activity more than the methyl group. Also the presence of a free carboxylic group as a C3-substituent was essential for the antibacterial activity.



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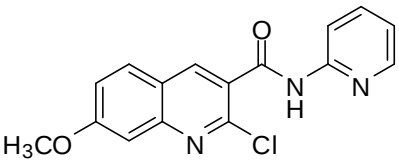

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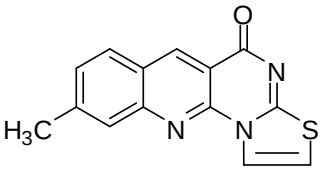

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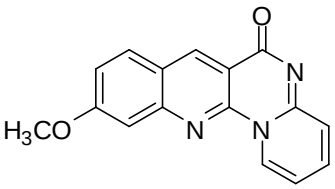

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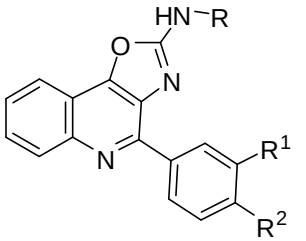
Anti tubercular agents:

S.Eswaran et al[14] have synthesized 4-(3 and 4 fluoro phenyl)-N-(Substituted phenyl) [1, 3] oxalo [4, 5-c] quinoline 2-amines **(12)**. The presence of aryl ring at second position of quinoline moiety gives a very good antibacterial and antitubercular activity. These are evaluated for their *in vitro* antibacterial activity against *Escherichia coIi* (ATTC-25922), *Staphylococcus aureus* (ATTC-25923), *Pseudomonas aeroginosa* (ATTC-27853) and *Klebsiella pneumoniae* and antitubercular activity against *M. tuberculosis* H37Rv (ATTC-27294).[12]



R = Alkyl/aralkyl/ aryl

R^1/R^2 = Fluoro

(12)

S. Eswaran et al[15] have reported Mefloquine derivatives as a new class of antitubercular molecules. Mefloquine is well-known antimalarial drug based on this molecule a number of its analogues are synthesized and shown to possess very good antibacterial and antituberculosis activities[15].

PLAN OF WORK

Inspired by the diverse biological activities of quinoline and hydrazones independently, the present study proposes to synthesise and evaluate the biological profile of quinolinylhydrazone derivatives. The proposed plan of synthesis of title compounds is presented below

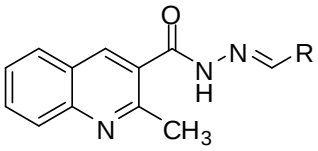
STEP 1: Synthesis of quinoline ester from o-nitro benzaldehyde and β-keto esters.

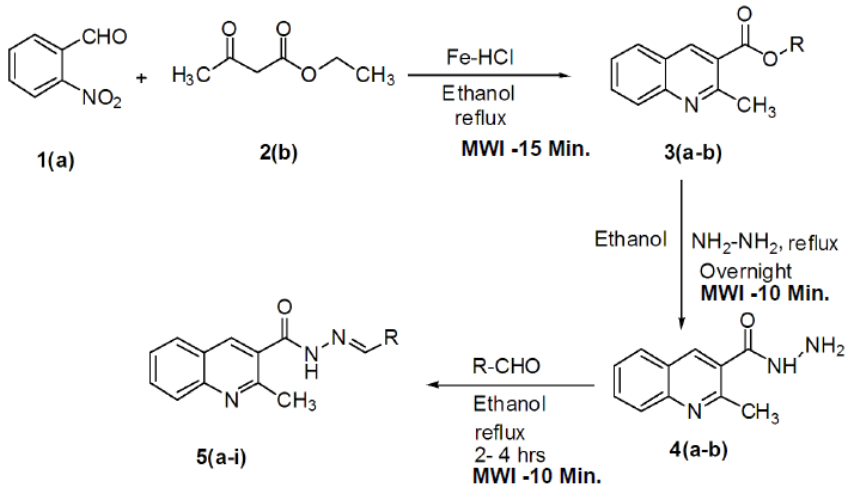
STEP 2: Synthesis of quinoline hydrazides from quinoline esters.

STEP3: Synthesis of quinolinylhydrazones by condensation of various aldehydes.

Literature survey reveals various methods for synthesis of quinolines which are presented in detail in the following paragraphs.

Structures and IUPAC names of the Quinoline Hydrazones

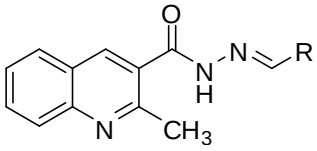




R = -C_6H_5(a), -$CH_3C_6H_4$(b), -$OCH_3C_6H_4$(c), -ClC_6H_4(d), -BrC_6H_4(e), -FC_6H_4(f), -$NO_2C_6H_4$(g), -FuranC_6H_4(h), -ThiopheneC_6H_4(i).

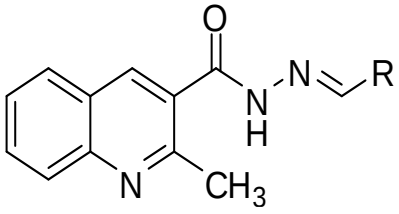
S.no	Product	R	IUPAC Name
1	**5a**	C_6H_5-	Benzylidene-2-methylquinoline-3-carbohydrazide
2	**5b**	4-CH_3-C_6H_4-	2-methyl-N'-(4-methylbenzylidene)quinoline-3-carbohydrazide
3	**5c**	4-OCH_3-C_6H_4-	N'-(4-methoxybenzylidene)-2-methylquinoline-3-carbohydrazide
4	**5d**	4-F-C_6H_4-	N'-(4-chlorobenzylidene)-2-methylquinoline-3-carbohydrazide
5	**5e**	4-Cl-C_6H_4	N'-(4-bromobenzylidene)-2-methylquinoline-3-carbohydrazide
6	**5f**	4-Br-C_6H_4	N'-(4-fluorobenzylidene)-2-methylquinoline-3-carbohydrazide
7	**5g**	4-NO_2-C_6H_4	2-methyl-N'-(4-nitrobenzylidene)quinoline-3-carbohydrazide
8	**5h**	2 - Furanyl	N'-(Furan-2-ylmethylene)-2-methylquinoline-3-carbohydrazide
9	**5i**	2 - Thiophenyl	2-methyl-N'-(thiophen-2-ylmethylene)quinoline-3-carbohydrazide

Physical data of *N*-alkylidene-2-methylquinoline-3-Carbohydrazide



S.no	R	Mol. formula	Mol. weight	Yield (%)by Conventional	Yield (%)by MWI	M.p (^{0}C)
1.	C_6H_5-	$C_{18}H_{15}N_3O$	289	92.3	98	182-184
2.	4-CH_3-C_6H_4-	$C_{19}H_{17}N_3O$	303	89.1	94	204-206
3.	4-OCH_3-C_6H_4-	$C_{19}H_{17}N_3O_2$	319	90.2	96	170-172
4.	4-F-C_6H_4-	$C_{18}H_{14}N_3OF$	307	91.1	95	180-183
5.	4-Cl-C_6H_4	$C_{18}H_{14}N_3OCl$	323	89.5	92	210-212
6.	4-Br-C_6H_4	$C_{18}H_{14}N_3OBr$	368	88.9	93	215-217
7.	4-NO_2-C_6H_4	$C_{18}H_{14}N_4O_3$	334	92.4	95	200-202
8.	2 – Furanyl	$C_{16}H_{13}N_3O_2$	279	93.6	97	202-204
9.	2 – Thiophenyl	$C_{16}H_{13}N_3OS$	295	91.7	96	230-232

Spectral data of quinoline hydrazones:



S.no	R	^{1}H NMR (DMSO-d_6 300 MHz) δ ppm	Mass (ESI):m/z	IR (KBr Disc) in cm^{-1}
1.	C_6H_5-	11.69 (1H, s), 8.29 & 8.15 (1H, s, Cis-trans conformer), 8.17-7.47 (1H, m), 7.88-7.61 (3H, m), 7.57-7.47 (1H, q), 7.42-7.32 (2H, m), 7.24 (2H, d), 2.85 & 2.73 (3H, s, Cis-trans conformer).	290$(M+H)^+$	
2.	4-CH_3-C_6H_4-	11.76 & 11.68 (1H, s, Cis-trans conformers), 8.30 & 8.25 (1H, s, Cis-trans conformer), 7.98 (1H, d),7.91-7.60 (4H, m), 7.53 (1H ,t), 7.22 (2H, t), 7.03 (1H, d), 2.83(3H, s, Cis-trans Conformer), 2.40-2.29 (3H, s, Cis-trans Conformer)	304$(M+H)^+$ 330$(M+Na)^+$	3215(NH), 1651(C=O)

3.	4-OCH_3-C_6H_4-	8.30 & 8.24 (1H, s, Cis-trans Conformer), 7.99 (1H, d), 7.93-7.64 (4H, m), 7.55 (1H, t), 7.29 (1H, d), 6.91(1H, d),6.74 (1H, d), 3.85 & 3.75 (3H, s, Cis-trans Conformer), 2.83 & 2.70 (3H, s, Cis-trans Confomer).	320$(M+H)^+$ 342$(M+Na)^+$	3464(NH), 1666(C=O)
4.	2 - Thiophenyl	11.84 & 11.74 (1H, s, Cis-trans Conformer), 8.53 & 8.30 (1H, s, Cis-trans conformer), 8.18 (1H, d), 8.02-7.67 (3H ,m), 7.58-6.91 (4H, m), 2.81 & 2.70 (3H, s, Cis-trans Conformer)	296$(M+H)^+$ 318$(M+Na)^+$	
5.	2 - Furanyl	11.71 & 11.63 (1H, s, Cis-trans Confrmer), 8.27 & 8.24 (1H, s, Cis-trans Conformer), 7.99 (1H, t), 7.84 (1H, t), 7.73 (1H, q), 6.86 (1H, s), 6.51(1H, s)	280$(M+H)^+$ 302$(M+Na)^+$	
6.	4-Cl-C_6H_4	8.35 & 8.29 (1H, s, Cis-trans Conformer), 8.16 & 8.05 (1H, s, Cis-trans Conformer), 8.01-7.94 (2H, m), 7.80-7.69 (2H, t), 7.60-7.49 (1H, t), 7.44-7.21 (3H, m), 2.81 & 2.68 (3H, s, Cis-trans Conformer)	324$(M+H)^+$ 326$(M+2)^+$	
7.	4-Br-C_6H_4	11.85 & 11.87 (1H, s, Cis-trans Conformer), 8.33 & 8.28 (1H, s, Cis-trans Conformer), 8.07-7.82 (3H, m), 7.80-7.63 (2H, m), 7.61-7.47 (2H, m),7.36 (1H, d), 7.25 (1H, d), 2.82 & 2.69 (3H, s, Cis-trans Conformer)	368$(M+H)^+$ 370$(M+2)^+$	3184(NH), 1654(C=O)
8.	4-F-C_6H_4-	-	308$(M+H)^+$ 330$(M+Na)^+$	
9.	4-NO_2-C_6H_4	-	335$(M+H)^+$	

REFERENCES

1. Lilienkampf, J. Mao, B.Wan, Y.Wang, S.G. Franzblau, A.P. Kozikowski, *J. Med. Chem.,* **52** (2009) 2109.
2. P. Nasveld, S. Kitchener, *Trans. R. Soc. Trop. Med. Hyg.*, **99** (2005) 2.
3. P.A. Leatham, H.A. Bird, V. Wright, D. Seymour, A. Gordon, *Eur. J. Rheumatol.Inflamm.,* **6** (1983) 209.
4. W.A. Denny, W.R. Wilson, D.C. Ware, G.J. Atwell, J.B. Milbank, R.J. Stevenson. U.S Patent 7064117 (2006).
5. A. Mahamoud, J. Chevalier, A. Davin-Regli, J. Barbe, Jean-Marie Pages, *Curr. Drug Targ.,* **7** (2006) 843.
6. N. Muruganantham, R. Sivakumar, N. Anbalagan, V. Gunasekaran, J.T. Leonard, *Biol. Pharm. Bull.,* **27** (2004) 1683.
7. M.P. Maguire, K.R. Sheets, K. McVety, A.P. Spada, A. Zilberstein, *J. Med. Chem.,* **37** (1994) 2129.
8. W.D. Wilson, S.E. Patterson, R.L. Wydra, L. Janda, L. Strekowski, *Med.Chem.,* Res. **2** (1992) 102.
9. Abu-Hussen, A.A.A. *J.Coord.chem.*, **59** (2006)157.
10. Singh, K.Barwa, M.S.Tyagi, *P.Eur.J.Med.Chem*., **4** (2006)1.
11. Mladenova, R.Ignatova, M.Manalova, N.Petrova.T.Rashkov, *I.Eur.Polym.J.*, **38** (2002)989.
12. Sheoraj singh, Vikas Kumar, Ashok Kumar, Shalash Sharma, Piyush Dua., *Bull.Korean Chemical Society*., **31** (2010) 3605.
13. Ola A.El-Sayed, Badr A.Al-Bassam, Maher E.Hussein, *Arch.Pharm.Pharm.Med.Chem.* **9** (2002) 403.

14. S.Eswaran, A.Vasudeva Adikari, R.Ajay kumar, *Eur.J.Med.Chem.*, **45** (2010) 957.

15. S.Eswaran, A.Vasudeva Adikari, Imran H.Chowdary, Nishith K.pal, K.D.Thamas, *Eur.J.Med.Chem*., **45** (2010) 3374.