ORIGINAL RESEARCH PAPER
Volume - 9 | Issue - 8 | August - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

SYNTHESIS, CHARACTERIZATION & PHARMACOLOGICAL SCREENING OF NEWLY SYNTHESIZED QUINOLINE DERIVATIVES

Pharmacy

Piyush Yadav* Department of Pharmaceutical Chemistry, Prasad Institute of Technology, Jaunpur-222001, India. *Corresponding Author

Jyotsna Pandey Department of Pharmaceutical Chemistry, Hygia Institute of Pharmaceutical Education and Research, Lucknow-226021, India.

Braj Nandan Kishor Department of Pharmacology, Hygia Institute of Pharmaceutical Education and Research, Lucknow-226021, India.

Smita Verma Department of Pharmacology, Shambhunath Institute of Pharmacy, Prayagraj, 211012, India

Priya Mishra Department of bPharmaceutical Chemistry, Hygia Institute of Pharmaceutical Education and Research, Lucknow-226021, India.

ABSTRACT

A series of novel Quinoline derivatives have been synthesized. These derivetives were prepared from the formation of intermediates 2-chloroquinoline-3 carbaldehyde and tetrazolo[1,5-a]quinoline-4-carbaldehyde and amines. The intermediate 2-chloroquinoline-3 carbaldehyde was prepared from Vilsmeier- haack reagent. The use of Vilsmeier-Haack (VH) reagent (POCl3/DMF) for the formylation of a variety of both aromatic and heteroaromatic substrates is well documented. It is now used as a powerful synthetic tool for the construction of many heterocyclic compounds. In this reaction we have formed firstly Vilsemeier-haack reagent by DMF and POCl3 added drop wise at 0-50C with continuous sterring. With the help of Vilsemeier-haack reagent and acetanilide at 90-1000C formed 2-chloroquinoline-3 carbaldehyde and then with the help of 2-chloroquinoline-3 carbaldehyde, PTSA, NaN3 and ethanol formed tetrazolo[1,5-a]quinoline-4-carbaldehyde and then with the help of tetrazolo[1,5-a]quinoline-4-carbaldehyde and different amines and solvent formed various derivatives which have significant anti-inflammatory activity. The structures of derivatives have been confirmed by the IR, H1 NMR spectral data. The compounds showed anti-inflammatory activity.

KEYWORDS

2-chloroquinoline-3 carbaldehyde, Tetrazolo[1,5-a]quinoline-4-carbaldehyde, Amines, Vilsmeier-haack reagent (DMF+POCl3), PTSA, NaN3, anti-inflammtory activity.

INTRODUCTION:

Medicinal chemistry is an interesting field as it relates several scientific disciplines and allows for association with other scientists in developing and researching novel drugs. Medicinal chemists use the process of synthesizing novel pharmaceuticals. They also develop the processes by which obtainable pharmaceuticals are prepared. Medicinal chemists are focused on drug improvement and innovation and are concerned with the isolation of medicinal agents found in medicinal plants and the design of novel synthetic drug compounds. The majority of chemists work with a group of scientists from different branches, as well as biologists, chemists, toxicologists [1, 2], pharmacologists. With this team uses complicated analytical techniques to synthesize and test new drug compounds and to produce the most commercial and environmentally friendly means of production [3, 4]. A cyclic organic compound having all carbon atoms in ring formation is called as a carbocyclic compound. When at least one atom instead of carbon forms a part of the ring system then it is called as a heterocyclic compound [5]. Oxygen, sulfur and nitrogen are common heteroatoms but heterocyclic rings having other hetero atoms are also generally recognized. A huge number of heterocyclic compounds are famous and this number is increasing rapidly. Accordingly the literature on the subject is very enormous.

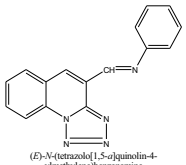
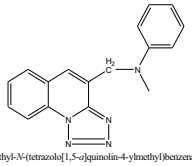
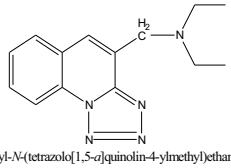
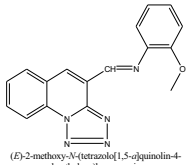
OBJECTIVE:

Quinoline nucleus is an important pharmacophore in medicinal chemistry, since a large number of its derivatives possess useful biological properties. Quinoline are known to possess Anti microbial (Jakkali Chandregowda Dharshan et al 2012), antidiabetic (L.Srikanth et al 2010), anti malerial (N. Kannappan et al 2009), antioxidant (Ramjith U. S et al 2013), diuretic (S.Venkataraman et al 2010), anticonvulsant (P.Y. Pawar et al 2013), antibacterial (Jalindar Jaware & Shobha et al 2014), antifungal (B.H.M. Jayakumar Swamy et al 2013), antimycobacterial (Alka Mital et al 2006) and anticancer (Lukasz Kaczmarek et al 2013). The quinoline ring is a frequent moiety present in various drug such as Abanoquil (α1-adrenergic receptor antagonist), 4 Aminoquinoline (antimalarial drugs), Amodiaquine (antimalarial and anti-inflammatory), Antrafenine (analgesic and anti-inflammatory), Bedaquiline (anti-tuberculosis), Broxyquinoline (antiprotozoal agent), Chloroquine (Prevention of malaria).

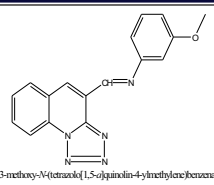
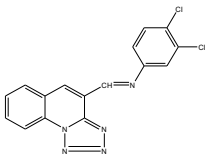
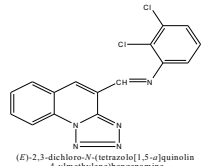
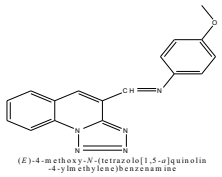
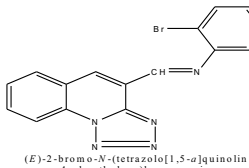
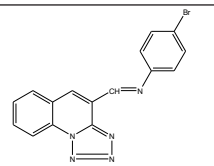
In view of the medicinal importance of quinoline nucleus as potential therapeutic agents, it was thought worthwhile to synthesize and characterized certain newer compounds having quinoline nucleus and evaluate for their biological potential.

METHODOLOGY:

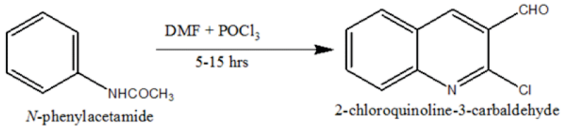
List of IUPAC Names of the synthesized compound

Compound Code	Structure with IUPAC Names
Jp1-1	 (*E*)-*N*-(tetrazolo[1,5-*a*]quinolin-4-ylmethylene)benzenamine
Jp1-2	 *N*-methyl-*N*-(tetrazolo[1,5-*a*]quinolin-4-ylmethyl)benzenamine
Jp1-3	 *N*-ethyl-*N*-(tetrazolo[1,5-*a*]quinolin-4-ylmethyl)ethanamine
Jp1-4	 (*E*)-2-methoxy-*N*-(tetrazolo[1,5-*a*]quinolin-4-ylmethylene)benzenamine

PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr

Jp1-5	 (*E*)-3-methoxy-*N*-(tetrazolo[1,5-*a*]quinolin-4-ylmethylene)benzenamine
Jp1-6	 (*E*)-3,4-dichloro-*N*-(tetrazolo[1,5-*a*]quinolin-4-ylmethylene)benzenamine
Jp1-7	 (*E*)-2,3-dichloro-*N*-(tetrazolo[1,5-*a*]quinolin-4-ylmethylene)benzenamine
Jp1-8	 (*E*)-4-methoxy-*N*-(tetrazolo[1,5-*a*]quinolin-4-ylmethylene)benzenamine
Jp1-9	 (*E*)-2-bromo-*N*-(tetrazolo[1,5-*a*]quinolin-4-ylmethylene)benzenamine
Jp1-9	 (*E*)-4-bromo-*N*-(tetrazolo[1,5-*a*]quinolin-4-ylmethylene)benzenamine

Synthesis of intermediate-



N-phenylacetamide — 2-chloroquinoline-3-carbaldehyde

Procedure-

Dry DMF (2.7 ML) is stirred with POCl3 (9 ml) at ice bath at 0-5 0C and then mixture was added with the N-phenylacetamide (1g). The mixture was stirred for 5-15 hrs on Magnetic stirrer with hot plate. On completion of reaction monitored by TLC. The mixture was kept at room temperature for 30 min. the mixture was poured in crushed ice and stirred for 1 hour, the solid crystal was filtered and wash with ice water and dreid. The compound was purified by recrystallisation from ethyl acetate.

Yield: 41.22%
m.p: 127-133 0C
Appearance: Vermilion crystal

Chemicals-

All the drugs used in this study were of pharmaceutical grade. Carrageenan was supplied by national chemical company, Vadodara. Diclofenac sodium was available in lab (HIPER, LKO.).

Animals-

Male wistar Albino rats weighing 100-200 g were used for Anti-inflammatory activity. They were housed in standard environmental condition like- ambient temperature (250C ± 10C), relative humidity (550C ± 5%), and 12/12hour light dark cycle. Animals had free access to standard pellet diet and water ad libitum. All animal experiments were carried out in accordance with the guidelines of CPCSEA. The institute animal ethical committee has given the approval for conducting animal experiment [6, 7].

Method-

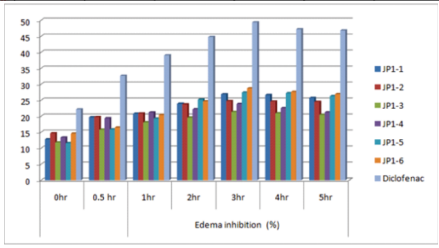
Anti- inflammatory activity was assessed by the method described by winter (winter et al, 1962). Male or female wister albino rats weighing (100-200g) were devided into 3 groups (N =3). Group 1 was kept as control and recived 0.2 ml of 1% carrageenan, Group 2 was kept as standard and received diclofenac (ref std 20mg/kg , oral), Group 3 was kept as the test and received test drug (20mg/kg, oral). Animals were treated with test drug and diclofenac subsequently1/2 hr after treatment, 0.2 ml of 1% suspension of carrageenan in normal saline was injected into the subplantar region of left hind paw to induce edema. The paw volume was measured at 0, ½, 1, 2, 3, 4, 5 hr after carrageenan injection using digital vernier calipus (Mitutoyo, Japan, HIPER, LKO.). The edema volume in the control group (Vc) and edema volumes in the group treated with test compounds (Vt) was measured and the percentage inhibiotion of edema was calculated using the formula [8, 9].

RESULT AND DISCUSSION:

The above works have been done on the quinoline nucleus. The synthesis of 2-chloroquinoline-3 carbaldehyde and tetrazolo[1,5-a]quinoline-4-carbaldehyde were prepared as intermediate followed by Vilsmeier-haach reagent. The anti-inflammatory activity was performed on Albino mice by inducing inflammatory reagent (normal saline + carrageenan). The data was analyzed by % inhibition compared to control and standard. The compounds JP1-5, JP1-6 showed potent anti-inflammatory activit y and others shoed less anti-inflammatory activity.

Table. Inhibitory effect of test compounds JP1-1 to JP1-6 and diclofenac upon carrageenan induced paw edema in rats-

Compound			Edema inhibition (%)				
	0hr	0.5 hr	1hr	2hr	3hr	4hr	5hr
JP1-1	12.80	19.67	20.81	23.92	26.88	26.63	25.74
JP1-2	14.69	19.75	20.89	23.72	24.77	24.63	24.50
JP1-3	11.80	15.80	18.09	19.57	21.33	20.91	20.45
JP1-4	13.36	19.41	21.19	22.19	23.86	22.56	21.23
JP1-5	11.58	15.89	19.30	25.20	27.42	27.22	26.30
JP1-6	14.58	16.49	20.43	24.66	28.69	27.63	26.92
Negative control							
Diclofenac	22.16	32.64	39.06	44.77	49.36	47.20	46.81



DISCUSSION:

The use of the Vilsmeier-Haack (VH) reagent (POCl3/DMF) for the formylation of both aromatic and heteroaromatic substrates is well recognized[10]. The Vilsmeier-Haack reagent is an efficient, cheap and mild reagent for the formylation of reactive aromatic and heteroaromatic substrates. It is used as an synthetic tool for the manufacture of lots of heterocyclic compounds. The Vilsmeier-Haack reaction, involves electrophilic substitution of an activated aromatic ring with a halomethyleniminium salt to yield the analogous iminium species, which facilitates simple entry into different nitrogen and oxygen based heterocycles[11]. Vilsmeier-haack reagent serves not only as a formylating agent, but also as an activating reagent for carboxylic acids to give esters, amides and acid chlorides and imides. Moreover this, the reagent has also been widely used for effecting a variety of chemical transformations with other classes of compounds[12].

CONCLUSION:

A series of 10 ring substituted tetrazolo[1,5-a]quinoline-4-carbaldehyde were prepared and characterized. All the derivatives were characterized by IR, H1-NMR and Elemental analysis. The prepared compounds were tested for anti-inflammatory activity. JP1-6

showed highest inhibition activity within the series.

REFERENCES:

1. GD Clayton, FE Clayton, 1994, "Patty's Industrial Hygiene and Toxicology Part E Toxicology", John Wiley & Sons Inc. New York, Vol-2, Page No. 3394-3397.
2. Janero, D.R. Malondialdehyde, 1999, "Thiobarbituric Acid Reactivity as Diagnostic Indices of Lipid Peroxidation and Peroxidative Tissue Injury", Free Radic. Biol. Med., Vol-9, Page No-515–540.
3. Pati Bibek* and Banerjee Subhasis, 2014, "Indispensability of Quinoline Moiety In The Field of Medicinal Chemistry Research-A Review", Journal of Pharma.sci.tech., Vol-3, Page No.59-67.
4. P. Patel Manish, and V Bhuva Sandip, 2012, "The Three Component One- Pot Synthesis and Biological Studies of Some New Octahydroacridine- 1,8- Dione Derivatives Containing Tetrazolo [1, 5-A] Quinoline Moiety", Indian J Chem, Vol-51B, Page No. 1388-1395.
5. Smith B. Michael and March Jerry, "March's Advanced Organic Chemistry", Wiley Student Edition, Sixth Edition, Chap. 16, Page No.1285.
6. T. Ashley Noah, M.Weil Zachary, and J. Nelson Randy, 2012, "Inflammation: Mechanisms, Costs, and Natural Variation", Annu. Rev. Ecol. Ecol. Syst., Vol- 43, Page No-385-406.
7. Mycek J. Mary, Harvey A. Richard, Pamela C. Champe, "Lippincott's Illustrated Reviews", Pharmacology 2nd edition, 401-419.
8. Kumar, Abbas, Aster, 2011, "Robbins Basic Pathology", Inflammation and Repair, Elsevier Saunders, 9th edition, Page No. 29-74.
9. Liao Jung-Chun, Tsai Jen-Chieh, Peng Wen-Huang*, Chiu Yung-Jia, Sung Ping-Jyun, Tsuzoki Minoru and Kuo Yueh-Hsiung*, 2013, "Anti-Inflammatory Activity of N-(3-Florophenyl)Ethylcaffeamide In Mice", Int. J. Mol. Sci., Vol- 14, Page No-15199-15211
10. Wiley E. C. John, 1976, "Advances in Organic Chemistry Iminium Salts in Organic Chemistry", New York Part I Taylor, Vol- 9, Page No. 225-342.
11. T. Hirota, H. Fujita, K. Sasaki, Namba, 1986, "T. J. Heterocycl. Chem.", Vol. 23, Page No. 1715.
12. Rajput AP* and Girase Pd, 2012, Review Article on Vilsmeier-Haack Reaction, IJPCBS, Vol-3, Page No. 25-43.