https://doi.org/10.33472/AFJBS.6.13.2024.1557-1570

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

SYNTHESIS AND PHARMACOLOGICAL SCREENING OF SUBSTITUTED PYRAZOLE-QUINOLINE DERIVATIVES

Md.Iliyas Bilagi[1], Somashekhar Metri[1], Shivanand Kolageri[1]

[1]Dept. of Pharmaceutical Chemistry, BLDEA's SSM College of Pharmacy and Research Centre, Vijayapura, Karnataka, India*

[1]csm.som@gmail.com

Article Info

Volume 6, Issue 13, July 2024

Received: 02 June 2024

Accepted: 30 June 2024

Published: 24 July 2024

doi: 10.33472/AFJBS.6.13.2024.1557-1570

ABSTRACT:

Three series of quinoline derivatives with pyrazole moiety have been developed in an effort to create novel antibacterial drugs. Have been synthesized from 2,8-dichloroquinoline-3-carbaldehyde converted into1-(2,8-dichloroquinoline-3-yl)-N-phenylmethanimine. Which is cyclised by hydrazine and conc.HCl to gives 1-(8-chloro-2-hydrazinylquinolin-3-yl)-N-phenylmethanimine it was reacted with ethylaceto acetate gives 1-{8-chloro-3-[(phenylimino)methyl]quinolin-2-yl)-3-methyl-1 H-pyrazol-5-ol derivatives. Hydrazides were created in order to try and reduce the resistance that arose as a result of the drug's decreased exocytosis concentration. These synthetic compounds underwent a preliminary biological assessment. Using IR, 1HNMR, and mass spectroscopy, the produced compounds were identified and characterized. By using the cup plate method to assess the compounds' antibacterial activity, MSBSM-VC and MSBSM-VE demonstrate notable antimicrobial activity.

KEYWORDS:-Pyrazole, Quinoline,analgesic and antimicrobial activity

1. INTRODUCTION

The azole class includes the aromatic heterocyclic system pyrazole. It is a pyrazole-containing ring with five members. Because the structures maintain aromaticity, they are the

most significant. three carbon atoms and two nitrogen atoms bonded together. Because its unshared electrons are conjugated with the aromatic system, the nitrogen atom (N1) is "pyrrole-like." Because the unshared electrons in nitrogen (N2) are not impaired by resonance, as they are in pyridine systems, the nitrogen atom is "pyridine-like." The variations in nitrogen atoms cause pyrazoles to react with both bases and acids [1-3].

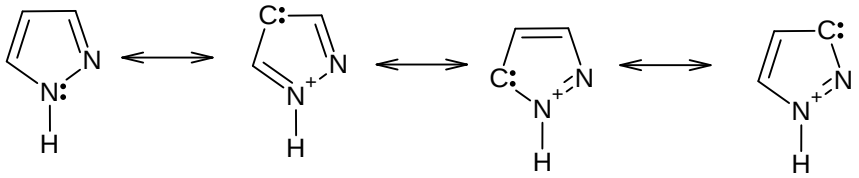
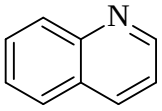


Fig: 1.1. Resonance structure of pyrazole

In medicinal chemistry, pyrazole derivatives have a well-established biological importance. Certain derivatives of pyrazoles have demonstrated antiviral, anticancer, anti-inflammatory, and antibacterial properties.and fungicidal activities [4-6].

1,5-functionalized pyrazoles hold a special place among the many medicinally significant pyrazole derivatives, and their assessment as antibacterial agents has garnered significant attention in the past. The biological activities are greatly enhanced when the aryl system is included into the pyrazole ring. Different substituents on the phenyl and pyrazole rings can significantly alter the biological characteristics of these compounds [7-11].

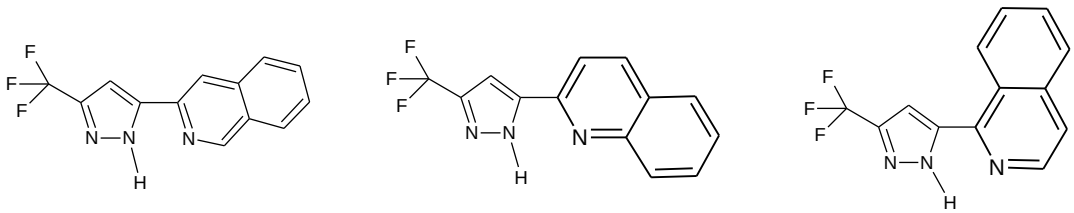
BRIEF REVIEW ON QUINOLINE



In light of the biological importance of these classes of compounds and as part of our ongoing research program on the synthesis of antimicrobial and analgesic agents, we intended to assemble these proven pharmacologically active nuclei into a combined molecular framework [12-14].

The deliberate construction of hybrid molecules comprising pharmacophoric subunits of two or more bioactive derivatives is known as molecular hybridization. A new hybrid scaffold may arise when two distinct molecules are joined with the aid of linkers. The intended hybrid chemicals would be less hazardous than the parent molecules and show increased potency, selectivity, and efficacy [15-17]

Through excellent manipulation of the π-conjugation structure, Chung et al. recently synthesized a series of quinoline−pyrazole (QP) isomers, which they then utilized to study the impact of π-conjugation on the excited state intramolecular proton transfer [18].

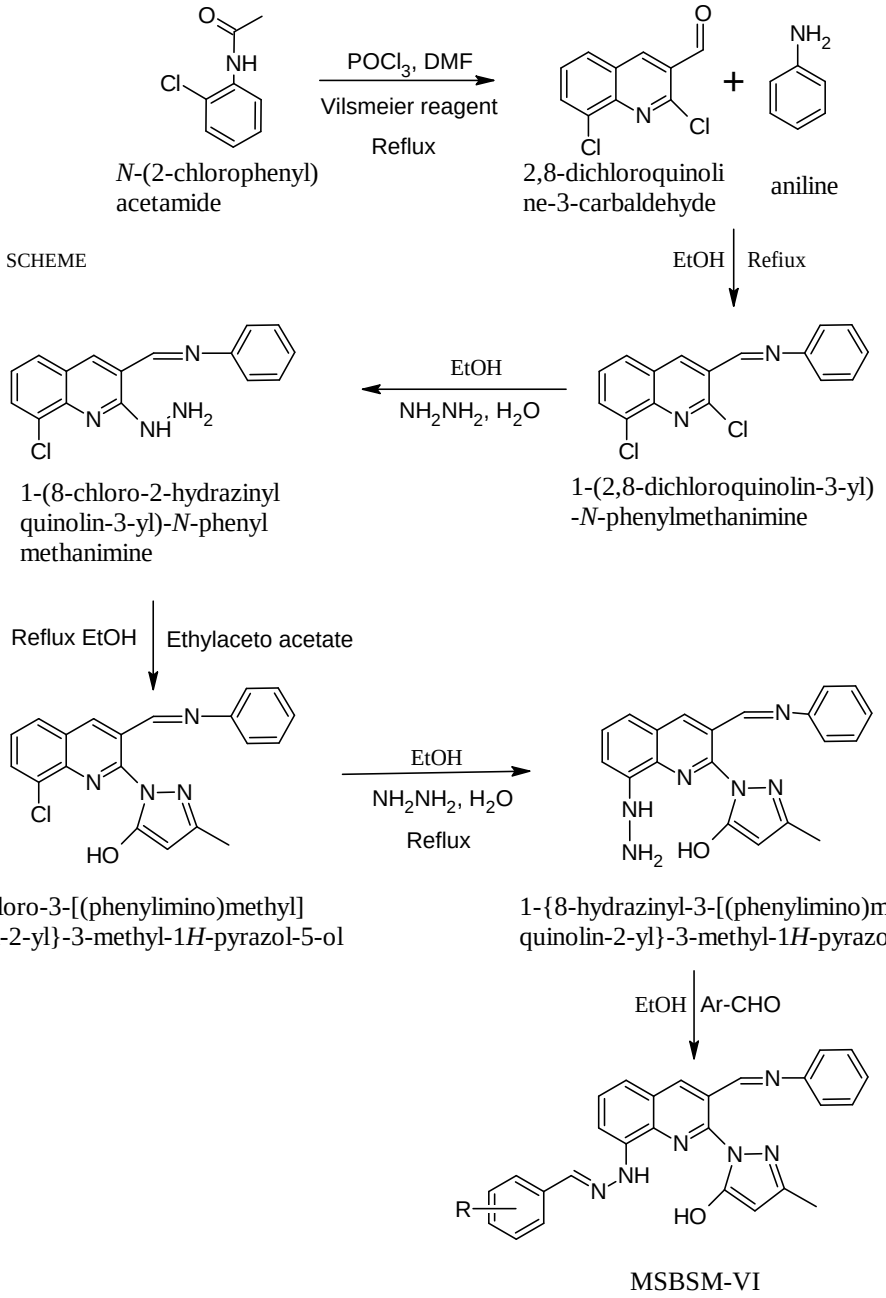


I II III

Fig 1.2 Molecular structures of Pyrazole-Quinoline isomerism

2. MATERIALS AND METHODES

N-(2-chlorophenyl) acetamide, Phosphorus oxychloride, N,N-Dimethylformamide(DMF), Vilsmeier reagent, Aniline, Ethanol, Ethylaceto acetate, alkyl halide, melting point apparatus, TLC, ^{1}H NMR, Mas spectroscop.



STEP-1: Preparation of compound 2,8-dichloroquinoline-3-carbaldehyde (MSBSM-I)

Phosporus oxychloride (0.35 mol, 53.55gm, 32.2ml) was added dropwise while stirring after N-(2-chlorophenyl)acetamide (0.125mol, 9.13gm, 9.65ml) had been cooled in a three-necked flask with a drying tube. The solution was heated under reflux for 16 hours at 85–90°C after 5 minutes. The response After the mixture had cooled, it was transferred to 300 milliliters of ice water and swirled for 30 minutes at 0 to 10. When the yellow precittate of 2,8-dichloroquinoline-3-carbaldehyde separated. The physicochemical properties were obtained by filtering, washing with cold water, drying, and recrystallizing the ethyl acetate, resulting in yellow, glossy, needle-shaped crystals.

STEP-2: Preparation of compound 1-(2,8-dichloroquinolin-3-yl)-N-phenylmethanimine (MSBSM-II)

Single-necked, round bottomed flask containing a 1.2cm x0.8cm egg shaped stir bar is charged sequentially and in one portion 2,8-dicholoroquinoline-3-carbaldehyde (10.4 ml) and aniline (9.75 ml) using a 3-ml plastic syringe through the septum with a vent needle. And reflux for 9 hours. 1-(2,8-dichloroquinolin-3-yl)-N-phenylmethanimine seperated into yellow precipitate. It was separated from the alcohol, dried, and cleaned with cold water. the qualities of physicochemistry.

STEP-3: Preparation of compound 1-(8-chloro-2-hydrazinylquinolin-3-yl)-N-phenylmethanimine (MSBSM-III)

In a round-bottom flask, add 10 ml of strong hydrochloric acid, 12 ml of hydrazine, and chill the liquid. Finally, add 20.2 gm (0.1mol) of 1-(2,8-dichloroquinolin-3-yl)-N-phenylmethanimine. Pour 40 milliliters of ethanol into crushed ice and let it reflux for eight hours while it's hot. Dry and filter the 1-(8-chloro-2-hydrazinylquinolin-3-yl)-N-phenylmethanimine product was confirmed by TLC and recrystallize form alcohol. The physicochemical properties.

STEP-4: Preparation of compound 1-{8-chloro-3-[(phenylimino)methyl]quinolin-2-yl}-3-methyl-1H-pyrazol-5-ol (MSBSM-IV)

Equimolar amounts of 1-(8-chloro-2-hydrazinylquinolin-3-yl)-N-phenylmethanimine then refluxed for five to six hours on a water bath in 25 milliliters of ethanol with a few drops of strong HCl. The reaction mixture was then cooled to room temperature and the 1-{8-chloro-3-[methyl (phenylimino)] quinolin-2-yl5-ol-3-methyl-1H-pyrazol The separated solid underwent filtering, petroleum ether washing, drying, and recrystallization from sutitable solvent. The synthetic substituted pyrazole's physical characteristics.

STEP-5: Preparation of compound 1-{8-hydrazinyl-3-[(phenylimino)methyl] quinolin-2-yl}-3-methyl-1H-pyrazol-5-ol (MSBSM-V)

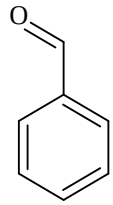
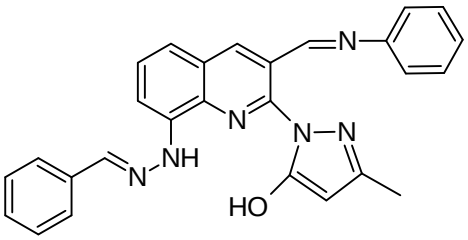
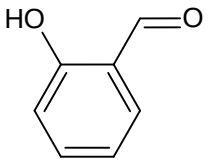
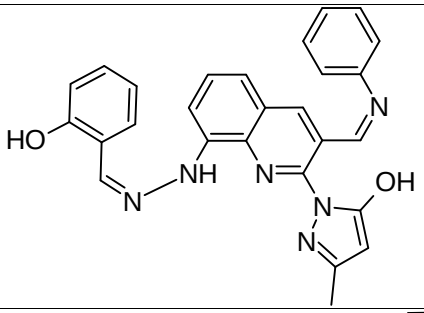
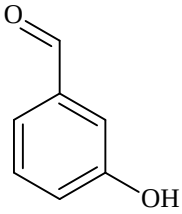
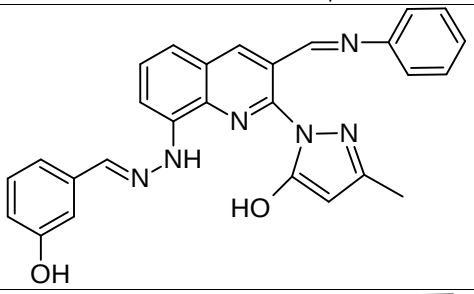
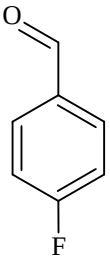
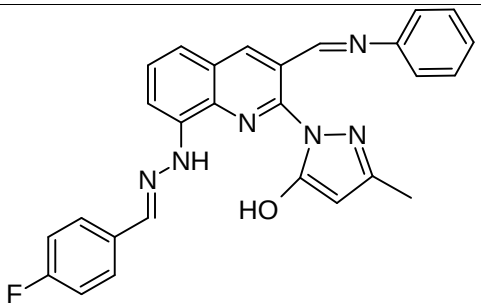
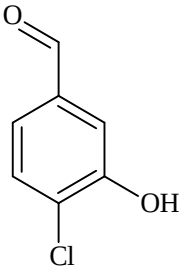
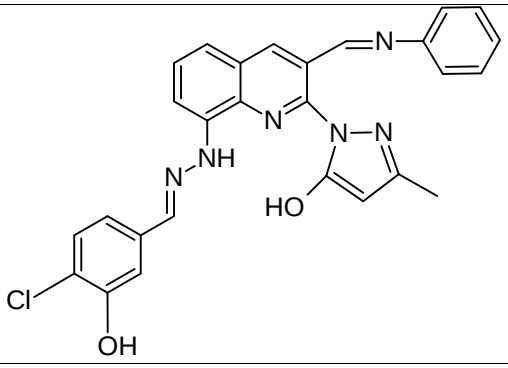
1-{8-chloro-3-[(phenylimino)methyl]quinolin-2-yl}-3-methyl-1H-pyrazol-5-ol in ethanol, hydrazine hydrate 100% was added dropwise with continuous stirring. After three hours of reflux, the reaction mixture was allowed to come to room temperature. Filtration, drying, and 1-{8-hydrazinyl-3-[(phenylimino)methyl] were done to the isolated solid.quinolin-2-yl5-ol-3-methyl-1H-pyrazol product was confirmed by TLC and crystallized from ethanol. The physicochemical properties.

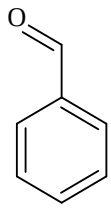
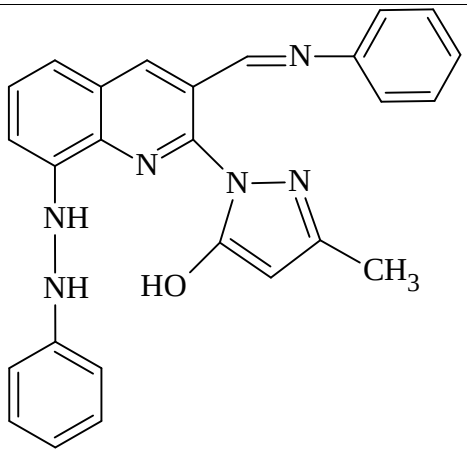
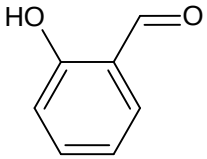
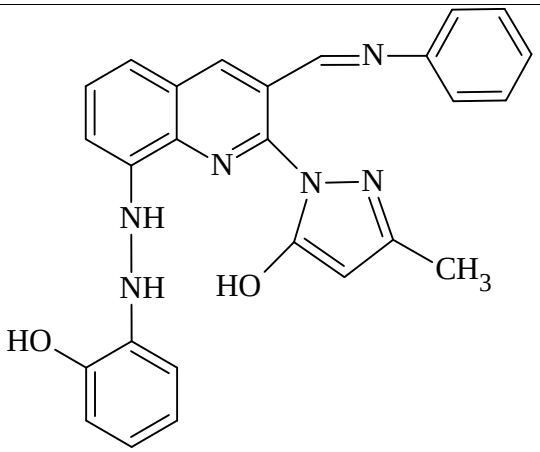
STEP-6: Preparation of compound 2-(5-hydroxy-3-methy-1H-pyrazol-1-yl)-8 (Phenylamino)quinoline-3-carbaldehyde (MSBSM-VI)

A 6-hour water bath reflux was used to combine 1-{8-hydrazinyl-3-[(phenylimino)methyl] quinolin-2-yl}-3-methyl-1H-pyrazol-5-ol (6gm, 1 mol) in ethanol (25 ml) and thionyl chloride (SOCl2) (3.3 ml, 0.5 mol). The excess thionyl chloride was eliminated by reduced pressure distillation or by gradually adding formic acid as needed, leaving a residue of 2-(5-hydroxy-3-methy-1H-pyrazol-1-yl)-8 (Phenylamino)quinoline-3-carbaldehyde." The next stage involved using the acquired data. Re-crystallization of the collected product.

Table No: 1.1 Substituted Aromatic Aldehyde and deivatives of 2-{[5-(pyridin-3-yl)-4*H*-1,2,4-triazol-3-yl]sulfanyl}acetohydrazide (MSBSM-VIA-VIG)

Compound Code	**Substituted Name with Structure**	**Derivatives procedure 1-{8-hydrazinyl-3-[(phenylimino)methyl] quinolin-2-yl}-3-methyl-1H-pyrazol-5-ol**

MSBSM-VIA	 Benzaldehyde	
MSBSM-VIB	 2-hydroxybenzaldehyde	
MSBSM-VIC	 3-hydroxybenzaldehyde	
MSBSM-VID	 4-fluorobenzaldehyde	
MSBSM-VIE	 4-chloro-3-hydroxybenzaldehyde	

MSBSM-VIF	 Benzaldehyde	
MSBSM-VIG	 2-hydroxybenzaldehyde	

3. RESULTS:

CHARACTERIZATION OF SYNTHESISED COMPOUNDS

To use spectroscopic methods such melting point, TLC, IR & 1HNMR, and mass spectrum studies to analyze pyrazole-quinoline derivatives in order to clarify their structure.

Melting Point of synthesized compounds

The melting point of the synthesised compounds was determined using the open capillary tube method. Because high-quality derivatives produce specific M.P., there were important criteria for determining the quality of synthesised derivatives. Because the quality assumption could not be met, any changes to the M.P. examination were required. When the melting point of a recrystallized compound is compared to that of a non-recrystallized compound, the melting point fluctuates only little.

Apparatus Thin Layer Chromatography

Thin layer chromatography was used largely to determine the purity and homogeneity of produced substances. Table No. 7 lists the solvents utilised. As an adsorbent, we employed Silica gel-G. Observation in UV light or exposure to iodine fumes were used to detect the presence of iodine. The following formula was used to obtain the RF value for each chemical.

$$Rf = \frac{Distances\ travelled\ by\ solute}{Distance\ travelled\ by\ the\ solvent\ front}$$

Infrared (Ir) Spectroscopy:-

Three smaller sections are typically distinguished within the IR region: near-IR (400 - 10 cm1), mid-IR (4000 - 400 cm-1), and far-IR (14000 – 4000 cm-1). The energy of infrared photons is sufficient to induce vibrations in atomic groups with respect to their bonding. Similar to electronic transitions, these vibrational transitions are correlated with specific energies, and only specific wavelengths and frequencies of infrared radiation are absorbed by

molecules. Chemical bonds have distinct frequencies of vibration; align their modes of vibration.

A spectrum that can be used to identify chemicals and functional groups is produced by measuring the radiation absorption as a function of frequency. In the infrared spectrum, certain contaminants generate distinct bands of their own. These bands' spectra are used to quantify the impurity concentration and how well they attach to the host material. Identification: A direct interpretation of the measured interferogram signal is not possible. One needs a way to "decode" each of the different frequencies. This can be achieved by using a well-known mathematical method known as transformation, which is carried out by the computer and provides the user with the required spectrum data for analysis.

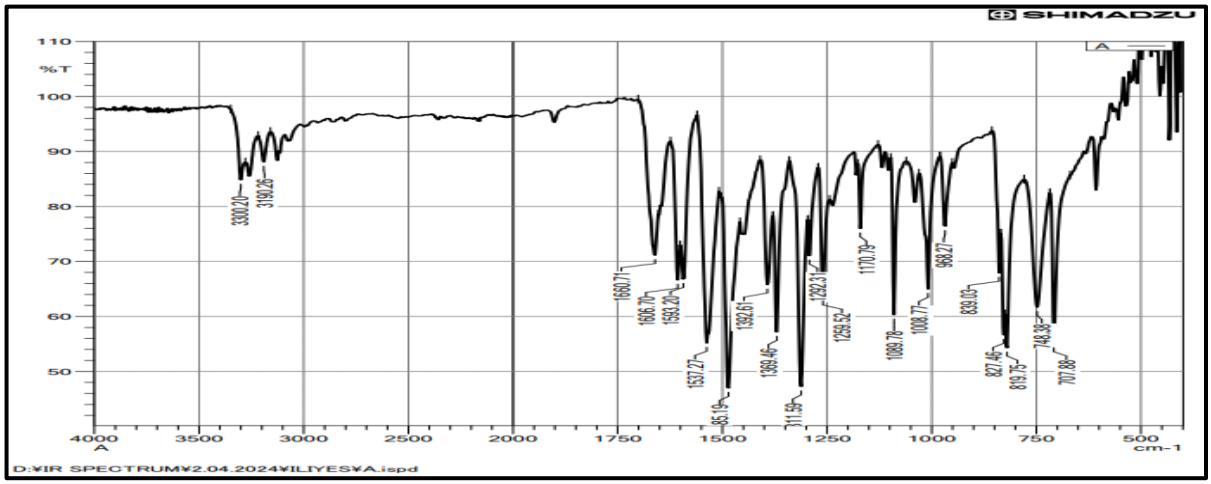
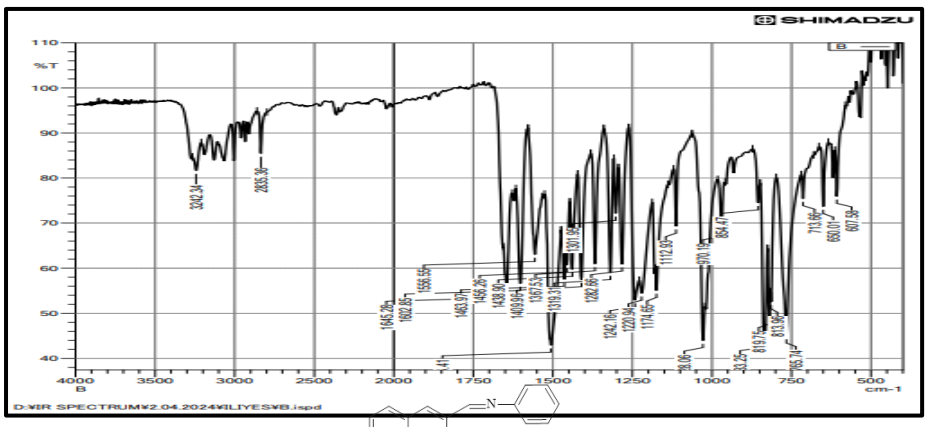


Figure No : 1.3 FTIR Spectrum of compound MSBSM-VIA

Table No: 1.2 FTIR Spectrum data of compound MSBSM-VIA

Types of Vibrations of Functional groups	**Group frequency in Wave number (KBr) cm^{-1}**
-NH Stretching	1593.20 cm^{-1}
Aromatic CH stretching	3190 cm^{-1}
Aliphatic CH	3328 cm^{-1}
C=N stretching	1089.78 cm^{-1}
OH stretching	3300.20 cm^{-1}



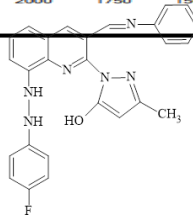


Figure No: 1.4 FTIR Spectrum data of compound MSBSM –VID

Table No: 1.3 FTIR Spectrum data of compound MSBSM-VIA

Types of Vibrations of Functional groups	**Group frequency in Wave number (KBr) cm^{-1}**
-NH Stretching	1556.55 cm^{-1}
Aromatic CH stretching	2835 cm^{-1}
Aliphatic CH	3240 cm^{-1}
C=O stretching	1112.93 cm^{-1}
OH stretching	3242.34 cm^{-1}
C-F stretching	970.19 cm^{-1}

BIOLOGICAL EVALVATION

❖ **Analgesic Activity:**

Acetic acid-induced Writhing in mice: Mice were divided into five groups, with five mice per group, for the mouse writhing assay. Writing was first introduced using Koster et al.'s methodology. 50, 100, and 200 mg/kg of pharmacological compounds were given intraperitoneally (i.p.) to the test group, whereas 0.3 ml of normal saline was given to the control group. The reference group was administered 100 mg/kg intraperitoneally.The therapies were given to the animals after a 16-hour fast. The mice were given an intraperitoneal injection (i.p.) of 0.3 ml of a 6% acetic acid solution an hour after treatment to cause writhing. 5 to 15 minutes following the acetic acid injection, the number of abdominal And it was calculated as follows.

Percentage inhibion = Wt(control)-Wt(test group) / Wt (control)

Wt = Mean Number of writhing

Table No 1.4: Analgesic activity of MSBSM-VIA-VIG

Sl. No	**Compound**	**% inhibition**
1	MSBSM-VIA	60.45***
2	MSBSM-VIB	48.12***
3	MSBSM-VIC	55.32***
4	MSBSM-VID	58.29***
5	MSBSM-VIE	58.12***
6	MSBSM-VIF	52.23***
7	MSBSM-VIG	20.02***
8	Indomethacin	80.70***

❖ **ANTI- MICROBIAL ACTIVITY:**

Anything that has the ability to destroy or stop the growth of bacteria, like extreme heat or chemicals, is considered an anti-microbial activity. Antibacterial substances fall into three main categories: disinfectants, antiseptics, and antibacterial medications. Bacteria are unicellular organisms that inhabit many environments. While bacteria might be beneficial in

some situations, they can also cause illnesses such bacterial pneumonia, most ear infections, and throat infections.

Antibacterial medications are applied to or within the bodies of organisms at relatively low concentrations in order to prevent or treat specific bacterial diseases without endangering the host organism. Antiseptics, disinfectants, and antibacterial medications are typically non-specific in their targeting; that is, they have the ability to either block or kill a wide range of microorganisms. Disinfectants are applied topically to objects or to water, while antiseptics are used topically in or on living tissue.

Chemotherapy using antibiotics is a crucial part of the treatment of many infectious disorders. On the other hand, overuse of some antibiotics might lead to resistance, which renders the medication useless against the microbe. The emergence of antimicrobial medication resistance has increased recently. We were inspired by this circumstance to develop a new line of antimicrobials.

The following can result in the development of drug resistance.

- Decreased drug intake,
- Increased drug efflux,
- Decreased drug delivery,
- Increased drug deactivation.
- Structure change at the intended location.
- Duplication of the target site's function.

EVALUATION OF ANTI-MICROBIAL ACIVITY:

The in vitro activity in pure cultures serves as the basis for determining anti-microbial activity. The cup-plate method is used to do in vitro susceptibility testing. By using the cup-plate method, the anti-microbial activity of pyrazole-quinoline derivatives was assessed against strains of common pathogens, including the gram-positive Enterococcus fecalis and the gram-negative Escherichia coli and Pseudomonas auriginosa. Ciprofloxacin is a common medication that is used at concentrations of 100µg and 200µg per milliliter.

METHOD OF TESTING

The technique is based on the diffusion of an antibiotic from a cavity through the petri dish's solidified agar layer to the point where the development of any additional microorganisms is completely stopped in a zone or circular area surrounding the cavity that holds a solution of test compounds. Molten nutritional agar (about 15–20 ml) was added to each sterilized petri plate. Using a sterile cork borer, nutritional agar was scooped out to create the cups. The agar plates that were created in this way were separated into distinct sets, and each set of plates was infected using a spread plate approach that involved a specific organism solution. Next, 0.1 ml of the test solution was added to the cups containing the inoculation plates Zone of inhibition (diameter in mm) produced on the plates, if any, was then measured for each organism and specific drug. To determine the solvent's activity, the solvent DMF was utilized as a negative control. The following Table provides a summary of the anti-microbial test results. The investigated compounds' activity is then measured by comparing them to that of the standard medication, ciprofloxacin.

Table No 1.5: Anti-microbial activity of MSBSM-VIA-VIG

Compound Code	**Diameter of the inhibition zone in millimeters (average triplicate ± standard deviation)**			
	P. aureus		**E. Coli**	
	250 µg	**500 µg**	**250 µg**	**500 µg**
MSBSM-VIA	18	21	18	20
MSBSM-VIB	17	21	15	19

MSBSM-VIC	15	20	20	19
MSBSM-VID	19	22	18	21
MSBSM-VIE	18	20	20	17
MSBSM-VIF	15	18	17	20
MSBSM-VIG	13	18	18	19
Ciprofloxacin	31	31	31	31

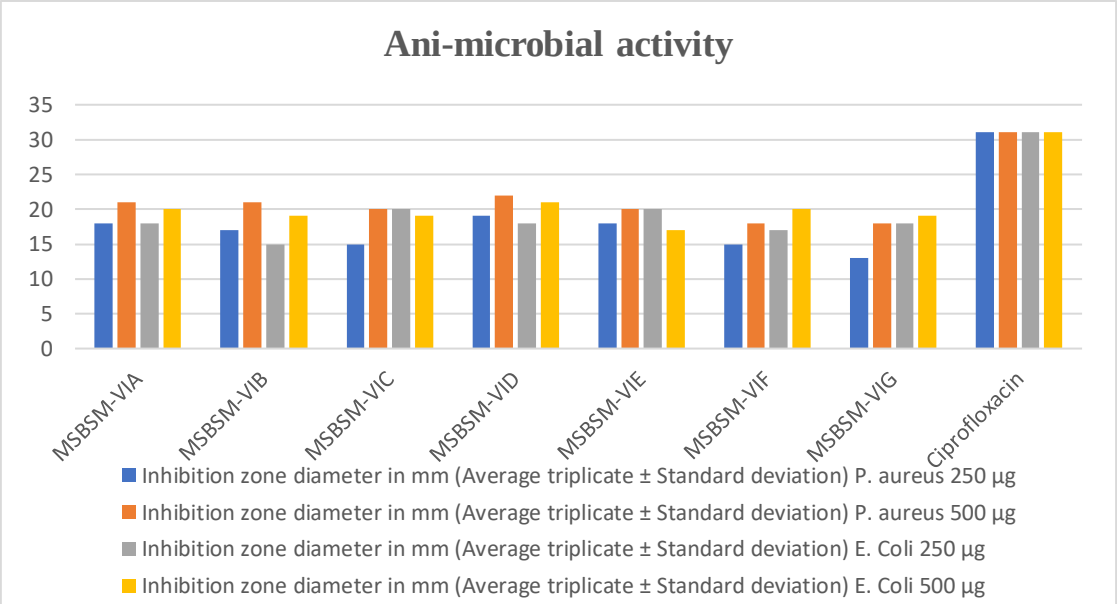


Figure No 1.5: Anti-microbial activity of MSBSM-VIA-VIG

4. DISCUSSION:

TLC was used to track every reaction and FTIR and physical constant studies were used to define the structures and purity of the expected compounds before 1H-NMR and mass spectroscopy were added. To consider the reaction complete, it was necessary to confirm that there were no TLC spots for the starting materials and that a new TLC single spot had appeared at a different Rf value. The TLC plates could be seen in a UV-visible chamber or by using iodine fumes. All of the reaction products were purified using various workup procedures to eliminate any unreacted starting components, and then they were recrystallized using the appropriate solvents. The majority of the procedures were refined to produce quantitative yields, or yields greater than 69%.

The intermediates yielded good yields and high purity after converting into the respective derivatives. The development of derivatives of the relevant structure is demonstrated by the FTIR investigations' peeks at -NH 1593.20 cm-1 stretch, C=N 1089.78 cm-1, and -OH 3300.20 cm-1. These derivatives will be evaluated for their biological activity. The manufactured derivatives compounds of Schemes MSBSM-VI analysis's H1 NMR spectrum and mass spectra data demonstrate that the resulting compounds can be further investigated for biological activity.

ANALGESIC ACTIVITY

Compounds which were selected in-vivo Analgesic activity were also screened for acetic acid induced analgesic activity.The tested compounds, All these compounds showed moderate analgesic activity compare to standard From this it is concern that the tested compounds have shown moderate analgesic activity in comparison with standard drug Indomethacin.

ANTI- MICROBIAL ACTIVITY:

Using the cup-plate method on nutrient agar media, all synthesized compounds were screened for antimicrobial activity studies at concentrations of 100 µg/ml and 200 µg/ml, with DMF serving as a control against Escherichia coli P. aureus. Ciprofloxacin, at concentrations of 100 µg/ml and 200 µg/ml, was the standard drug used for comparison against Gram positive and Gram-negative bacteria. The majority of the produced compounds are active against bacteria, according to the data in the table. While the remaining compounds.

5. CONCLUSION:

An overview of the pharmacological activities of Pyrazole-Quinoline, the fundamental nucleus. The current work's goal is to find evidence in the literature that pyrazole-quinoline derivatives have biological activity., keep this in view it is proposed to synthesis some new pyrazole-quinoline derivative. The synthesised compound are characterized by IR, 1HNMR and m spectroscopy. Basic study requirements are mentioned ass spectroscopy. Previous research pertaining to the planning and assessment of the synthesis of derivatives of pyrazole and quinolé has been published in a number of scientific journals. The goal of the current effort is to synthesize a novel pyrazole-quinoline derivative using scheme-1 from a survey of the literature.The chemicals, reagents, tools, techniques and procedures/methods used in the present research work are detailed given. The target molecules, which link the pyrazole and quinoline nuclei, were successfully synthesized. The TLC technique was used to check the compounds' purity, and the FT-IR, 1HNMR, and MASS spectrum data were used to confirm the structures. The substance is tested for its antibacterial and analgesic properties in vivo. The produced pyrazole-quinoline compounds' results of spectral analysis with IR, NMR, and antimicrobial activity are provided in detail. The conclusion of the synthesised and pharmacological activity of pyrazole-quinoline derivatives are made in this chapter.

The present study demonstrates that the Synthesized Novel Pyrazole-Quinoline derivatives are confirmed with TLC , ^{1}HNMR, Mass spectroscopical methods, which shows the Potent Analgesic activity which has screened by Acetic acid-induced Writhing in mice method. Even though the results obtained *in vivo* Analgesic Activity data reveals that the Novel synthesized Pyrazole-Quinoline derivatives possessed by the most of compounds are inferior to that of the standard drugs employed.

Potent Anti-microbial activity which has screened by **Cup plate** method. Even though the results obtained by this method Anti-microbial Activity data reveals that the Novel synthesized Pyrazole-Quinoline derivatives possessed by the most of compounds are inferior to that of the standard drugs employed.

The synthesised Pyrazole-Quinoline moieties can be a rich source for additional exploitation, as demonstrated by all of the previous studies.

Therefore, investigating the prospect of fusing distinct moieties in this area may be valuable in the hunt for next generation medications with high potency, selectivity, and lower toxicity. When used effectively, it could produce better chemicals.

ACKNOWLEDGEMENT

It is a pleasant duty to express my sincere grateful thanks to Associate Professor Dr. Somashekhar Metri, Asst. Professor, Mr. Shivanand kolageri and Mr. Sandeep Umarani Department of Pharmaceutical Chemistry for their precocious guidance and timely suggestion.

CONFLICT OF INTEREST:

No

6. REFRENCES

1. Nangare A, Randive D, Barkade G. Synthesis and Biological evaluation of Novel Quinazoline derivatives as Anticancer, Antibacterial and Antifungal agents. Bull. Env. Pharmacol. Life Sci. 2021 Mar 4;10:179-90.
2. Bae I, Kim D, Choi J, Kim J, Kim M, Park B, Kim YH, Ahn YG, Kim HH, Kim DK. Design, synthesis and biological evaluation of new bivalent quinazoline analogues as IAP antagonists. Bioorganic & Medicinal Chemistry Letters. 2021 Feb 15;34:127676.
3. Bansal R, Malhotra A. Therapeutic progression of quinazolines as targeted chemotherapeutic agents. European Journal of Medicinal Chemistry. 2021 Feb 5;211:113016.
4. Jamroskovic J, Doimo M, Chand K, Obi I, Kumar R, Brännström K, Hedenström M, Nath Das R, Akhunzianov A, Deiana M, Kasho K. Quinazoline ligands induce cancer cell death through selective STAT3 inhibition and G-quadruplex stabilization. Journal of the American Chemical Society. 2020 Jan 28;142(6):2876-88.
5. Li B, Li Z, Guo F, Song J, Jiang X, Wang Y, Gao S, Wang J, Pang X, Zhao L, Zhang Y. Realizing efficient single organic molecular white light-emitting diodes from conformational isomerization of quinazoline-based emitters. ACS Applied Materials & Interfaces. 2020 Feb 27;12(12):14233-43.
6. Saleh NM, El-Gazzar MG, Aly HM, Othman RA. Novel anticancer fused Pyrazole derivatives as EGFR and VEGFR-2 dual TK inhibitors. Frontiers in chemistry. 2020:917.
7. Osarumwense PO, Edema MO, Usifoh CO. Synthesis and Anagesic activities of Quinazolin-4 (3H)-One, 2-Methyl-4 (3H)-Quinazolinone and 2–Phenyl-4 (3H)-quinazolin-4 (3H)–one. Journal of Drug Delivery and Therapeutics. 2020 Aug 15;10(4-s):87-91.
8. Khodair AI, Alsafi MA, Nafie MS. Synthesis, molecular modeling and anti-cancer evaluation of a series of quinazoline derivatives. Carbohydrate Research. 2019 Dec 1;486:107832.
9. Metwally NH, Saad GR, Abd El-Wahab EA. Grafting of multiwalled carbon nanotubes with pyrazole derivatives: characterization, antimicrobial activity and molecular docking study. International journal of nanomedicine. 2019;14:6645.
10. Hassan GS, Rahman DE, Abdelmajeed EA, Refaey RH, Salem MA, Nissan YM. New pyrazole derivatives: Synthesis, anti-inflammatory activity, cycloxygenase inhibition assay and evaluation of mPGES. European journal of medicinal chemistry. 2019 Jun 1;171:332-42.
11. Dai H, Huang M, Qian J, Liu J, Meng C, Li Y, Ming G, Zhang T, Wang S, Shi Y, Yao Y. Excellent antitumor and antimetastatic activities based on novel coumarin/pyrazole oxime hybrids. European journal of medicinal chemistry. 2019 Mar 15;166:470-9.
12. Farag AM, Fahim AM. Synthesis, biological evaluation and DFT calculation of novel pyrazole and pyrimidine derivatives. Journal of Molecular Structure. 2019 Mar 5;1179:304-14.
13. Chavan RR, Hosamani KM. Microwave-assisted synthesis, computational studies and antibacterial/anti-inflammatory activities of compounds based on coumarin-pyrazole hybrid. Royal Society open science. 2018 May 2;5(5):172435.
14. Nossier ES, Fahmy HH, Khalifa NM, El-Eraky WI, Baset MA. Design and synthesis of novel pyrazole-substituted different nitrogenous heterocyclic ring systems as potential anti-inflammatory agents. Molecules. 2017 Apr;22(4):512.
15. Ahn M, Gunasekaran P, Rajasekaran G, Kim EY, Lee SJ, Bang G, Cho K, Hyun JK, Lee HJ, Jeon YH, Kim NH. Pyrazole derived ultra-short antimicrobial peptidomimetics

with potent anti-biofilm activity. European journal of medicinal chemistry. 2017 Jan 5;125:551-64.
16. B'Bhatt H, Sharma S. Synthesis and antimicrobial activity of pyrazole nucleus containing 2-thioxothiazolidin-4-one derivatives. Arabian Journal of Chemistry. 2017 May 1;10:S1590-6.
17. Datar PA, Jadhav SR. Design and synthesis of pyrazole-3-one derivatives as hypoglycaemic agents. International Journal of Medicinal Chemistry. 2015;2015.
18. Rai US, Isloor AM, Shetty P, Pai KS, Fun HK. Synthesis and in vitro biological evaluation of new pyrazole chalcones and heterocyclic diamides as potential anticancer agents. Arabian Journal of Chemistry. 2015 May 1;8(3):317-21.
19. Xu YL, Lin HY, Ruan X, Yang SG, Hao GF, Yang WC, Yang GF. Synthesis and bioevaluation of pyrazole-benzimidazolone hybrids as novel human 4-Hydroxyphenylpyruvate dioxygenase inhibitors. European Journal of Medicinal Chemistry. 2015 Mar 6;92:427-38.
20. Kamal A, Shaik AB, Jain N, Kishor C, Nagabhushana A, Supriya B, Kumar GB, Chourasiya SS, Suresh Y, Mishra RK, Addlagatta A. Design and synthesis of pyrazole–oxindole conjugates targeting tubulin polymerization as new anticancer agents. European journal of medicinal chemistry. 2015 Mar 6;92:501-13.
21. Sangani CB, Makawana JA, Zhang X, Teraiya SB, Lin L, Zhu HL. Design, synthesis and molecular modeling of pyrazole–quinoline–pyridine hybrids as a new class of antimicrobial and anticancer agents. European Journal of Medicinal Chemistry. 2014 Apr 9;76:549-57.
22. Mohareb RM, Abdallah AE, Abdelaziz MA. New approaches for the synthesis of pyrazole, thiophene, thieno [2, 3-b] pyridine, and thiazole derivatives together with their anti-tumor evaluations. Medicinal Chemistry Research. 2014 Feb;23(2):564-79.
23. Vijesh AM, Isloor AM, Shetty P, Sundershan S, Fun HK. New pyrazole derivatives containing 1, 2, 4-triazoles and benzoxazoles as potent antimicrobial and analgesic agents. European Journal of Medicinal Chemistry. 2013 Apr 1;62:410-5.
24. Dawood KM, Eldebss TM, El-Zahabi HS, Yousef MH, Metz P. Synthesis of some new pyrazole-based 1, 3-thiazoles and 1, 3, 4-thiadiazoles as anticancer agents. European journal of medicinal chemistry. 2013 Dec 1;70:740-9.
25. Hassan SY. Synthesis, antibacterial and antifungal activity of some new pyrazoline and pyrazole derivatives. Molecules. 2013 Mar;18(3):2683-711.
26. Malladi S, Isloor AM, Isloor S, Akhila DS, Fun HK. Synthesis, characterization and antibacterial activity of some new pyrazole-based Schiff bases. Arabian Journal of Chemistry. 2013 Jul 1;6(3):335-40.
27. Horrocks P, Pickard MR, Parekh HH, Patel SP, Pathak RB. Synthesis and biological evaluation of 3-(4-chlorophenyl)-4-substituted pyrazole derivatives. Organic & Biomolecular Chemistry. 2013;11(29):4891-8.
28. Kumar P, Chandak N, Kaushik P, Sharma C, Kaushik D, Aneja KR, Sharma PK. Synthesis and biological evaluation of some pyrazole derivatives as anti-inflammatory–antibacterial agents. Medicinal Chemistry Research. 2012 Nov;21(11):3396-405.
29. Mohamed MF, Mohamed MS, Shouman SA, Fathi MM, Abdelhamid IA. Synthesis and biological evaluation of a novel series of chalcones incorporated pyrazole moiety as anticancer and antimicrobial agents. Applied biochemistry and biotechnology. 2012 Nov;168(5):1153-62.
30. Selvam TP, Saravanan G, Prakash CR, Kumar PD. Microwave-Assisted synthesis, characterization and biological activity of novel pyrazole derivatives. Asian Journal of Pharmaceutical Research. 2011;1(4):126-9.

31. Magda AA, Abdel-Aziz NI, Alaa AM, El-Azab AS, Asiri YA, ElTahir KE. Design, synthesis, and biological evaluation of substituted hydrazone and pyrazole derivatives as selective COX-2 inhibitors: Molecular docking study. Bioorganic & medicinal chemistry. 2011 Jun 1;19(11):3416-24.
32. Castagnolo D, De Logu A, Radi M, Bechi B, Manetti F, Magnani M, Supino S, Meleddu R, Chisu L, Botta M. Synthesis, biological evaluation and SAR study of novel pyrazole analogues as inhibitors of Mycobacterium tuberculosis. Bioorganic & medicinal chemistry. 2008 Sep 15;16(18):8587-91.
33. Nidhar M, Khanam S, Sonker P, Gupta P, Mahapatra A, Patil S, Yadav BK, Singh RK, Tewari AK. Click inspired novel pyrazole-triazole-persulfonimide & pyrazole-triazole-aryl derivatives; Design, synthesis, DPP-4 inhibitor with potential anti-diabetic agents. Bioorganic Chemistry. 2022 Jan 6:105586.
34. Basavanna V, Chandramouli M, Bhadraiah UK, Shettar AK, Doddamani S, Ningaiah S. Novel (Quinolin-8-yl-oxy)-pyrazole/thiophene Derivatives: Synthesis, Characterization and their Pharmacological Evaluation. Results in Chemistry. 2022 Jan 4:100281.
35. Cherukumalli PK, Tadiboina BR, Gulipalli KC, Bodige S, Badavath VN, Sridhar G, Gangarapu K. Design and synthesis of novel urea derivatives of pyrimidine-pyrazoles as anticancer agents. Journal of Molecular Structure. 2022 Mar 5;1251:131937.