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SYNTHESIS AND EVALUATION OF PHARMACOLOGICAL ACTIVITIES OF PYRIMIDINE BASED DERIVATIVES

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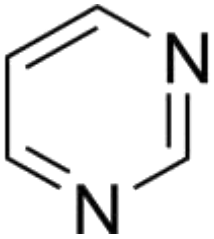
ABSTRACT

Nitrogen containing synthetically and biologically important heterocyclic ring system namely pyrimidine possess both biological and pharmacological activities and defend as aromatic six heterocyclic with 1 and 3 nitrogen atom in ring. Preparation of pyrimidine via different methods offer its importance in fields of medicinal chemistry and chemistry. Pyrimidines and their derivatives act as anti-inflammatory, anti-malaria, anti-tumor. cardiovascular agents, anti-neoplastic. anti-tubercular, anti-HIV, diuretic, anti-viral, anti-microbial, analgesic. This project give light up on biological and pharmacological activities of pyrimidine nucleus. Pyrimidine is an imperative heterocyclic ring, and as a part of various pharmacophores, it presents a diverse spectrum of biological activities making it valuable in medicinal chemistry. As a result, there is a never-ending hunt for an environmentally sustainable method of its synthesis. Applying green approaches for producing heterocyclic substituted pyrimidine derivatives could aid in the discovery of new drug candidates.

KEYWORDS:

Antioxidant. Antimicrobial. Antibacterial, Antifungal, Antiviral, Pyrimidine derivatives.

INTRODUCTION



Pyrimidine, an aromatic heterocycle, contains two nitrogen atoms in the ring at 1st and 3rd positions. In 1984 Pinner studied pyrimidines systematically by synthesizing derivatives through condensation of ethyl acetoacetate with amidines and first proposed the name “pyrimidin” in 1885. In 1900 Gabriel and Colman synthesized 2,4,6-trichloropyrimidine from barbituric acid which was then reduced by zinc dust in hot water to give the parent compound.(2)

Pyrimidine is an imperative heterocyclic ring, and as a part of various pharmacophores, it presents a diverse spectrum of biological activities making valuable in medicinal chemistry. As a result, there is a never-ending hunt for an environmentally sustainable method of its synthesis. Pyrimidine derivatives are a class of heterocyclic compounds that have been widely studied for their diverse pharmacological activities.(1) These compounds have been found to exhibit antimicrobial, anti-inflammatory, antioxidant, and anticancer properties, making them potential candidates for the development of new drugs.

The need for developing new eco-friendly methods which includes spectacular reduction in reaction time, clean product formation, improved selectivity and yields and easier work up is currently a focus of attention in organic synthesis. The use of microwave irradiation for the synthesis of new compounds has proved to be efficient, safe, and environmentally benign due to its ability to fuse starting materials directly and high thermal conductivity leading to a rapid increase in the temperature of the reaction. Also, delayed rise in temperature enhances the probability of generating side products.

Biological significance of pyrimidine is:

Pyrimidines are essential building blocks of life with diverse biological roles. They are found in:

1.Nucleic Acids: Cytosine, thymine, and uracil are pyrimidines that form the core of

DNA and RNA, carrying genetic information.

2.Vitamins: Thiamine (Vitamin B1) contains a pyrimidine ring and is crucial for energy metabolism.

3.Coenzymes: Pyrimidine nucleotides are involved in various enzymatic reactions and cellular processes.

Therapeutic Applications:

1. Anticancer agents: Pyrimidine derivatives have shown promise as anticancer agents, targeting various types of cancer cells.

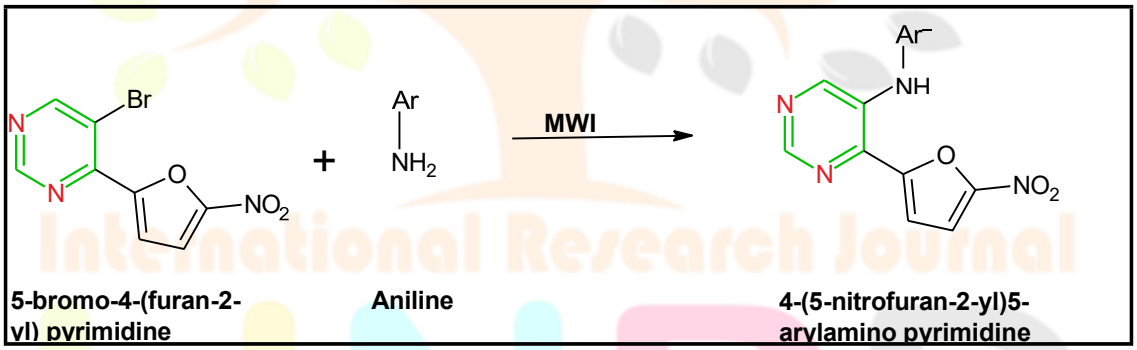
2. Antimicrobial agents: These compounds exhibit antimicrobial activity, making them potential treatments for bacterial, viral, and fungal infections.

3. Anti-inflammatory agents: Pyrimidine derivatives have been found to possess anti-inflammatory properties, which could be beneficial in treating inflammatory diseases.

4. Antiviral agents: Some pyrimidine derivatives have demonstrated antiviral activity, particularly against certain viral infections.(6)

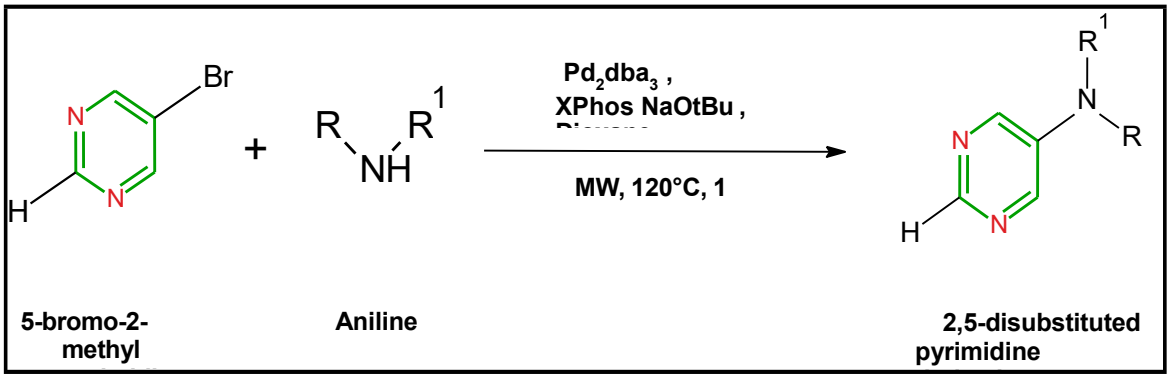
LITERATURE REVIEWS

Verbitskiy *et al* described the microwave irradiation assisted synthesis of 4-(5-nitrofuran- 2-yl)-5-arylamino substituted pyrimidines. Arylamination of 5-bromo-4-(furan-2- yl)pyrimidine and various anilines was carried out in the presence of 20 mol% Pd(OAc)2 as catalyst, employing Buchwald–Hartwig amination reaction at 250W , 150°C for 10 minutes. The synthetic scheme is described in **Scheme 1.**



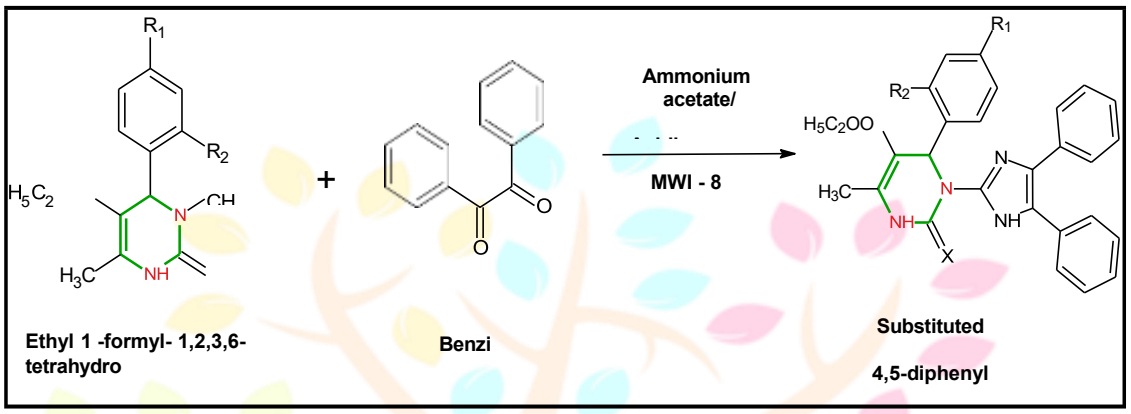
Scheme 1. Synthesis of 4-(5-nitrofuran-2-yl)-5-arylamino substituted pyrimidines

Li *et al* demonstrated microwave irradiation assisted synthesis of 2,5-disubstituted pyrimidine derivatives by amination of 2,5-disubstituted pyrimidine using a 5-bromo-2- methylpyrimidine and anilines. The Buchwald-Hartwig amination reaction was employed, in the presence of palladium catalysts with XPhos and Cs_2CO_3 in 1,4-dioxane, for 1 hr at 120°C with 82% yield. The synthetic scheme is described in **Scheme 2.**



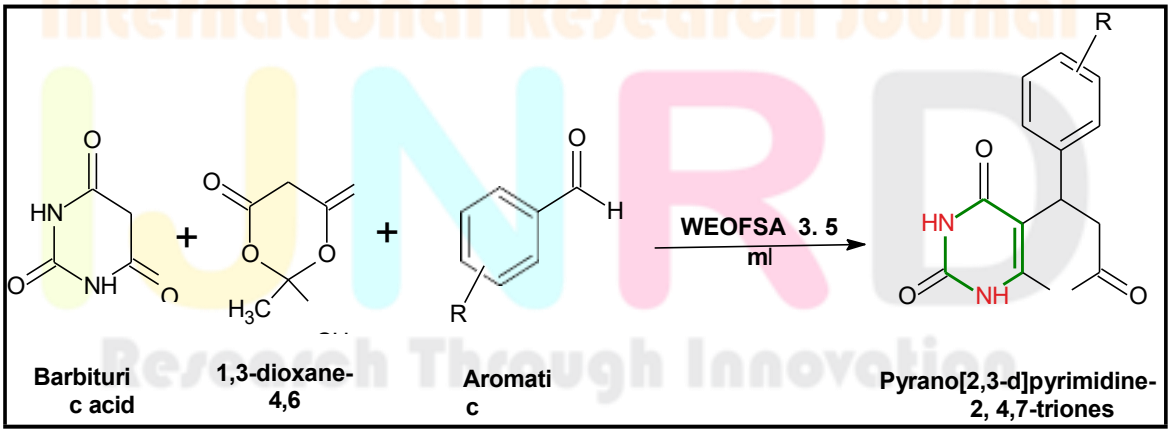
Scheme 2. Synthesis of 2,5-disubstituted pyrimidine derivatives

Khatavi *et al* demonstrated a microwave irradiation assisted synthesis of pyrano[2,3-*d*]pyrimidine-2,4,7-triones from barbituric acid, 1,3-dioxane-4,6-dione, andaromatic aldehyde. Reaction was carried out under the microwave irradiation of 450W and catalyzed by a 10% water extract of Orange Fruit Shell Ash (WEOFSA) (*Citrus sinensis*) extract. The synthetic scheme described in **Scheme 3.**



Scheme 3. Synthesis of pyrano[2,3-*d*]pyrimidine-2,4,7-triones

Rahatgaonkar *et al* developed a microwave assisted synthesis of substituted 4,5-diphenyl imidazolyl pyrimidine hybrids from ethyl 1- formyl- 1,2,3,6- tetrahydro -4- methyl-6- phenyl-2-oxo/thioxopyrimidine-5-carboxylates (25 mmol), Benzil (25 mmol), ammonium acetate and acidic alumina, which were reacted under microwave irradiation for 8 minutes to give the product in high yields.



Scheme 4. Synthesis of substituted 4,5-diphenyl imidazolyl pyrimidine

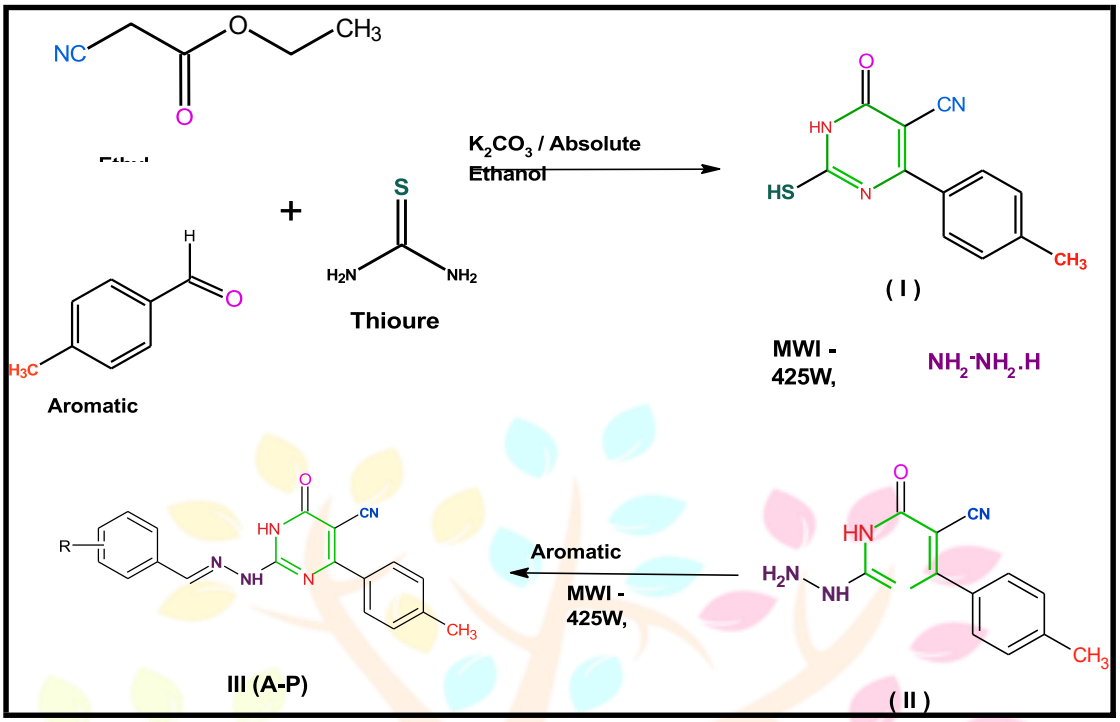
AIM & OBJECTIVE

Aim: To synthesize and evaluate biological activities of pyrimidine derivative.

Objectives:

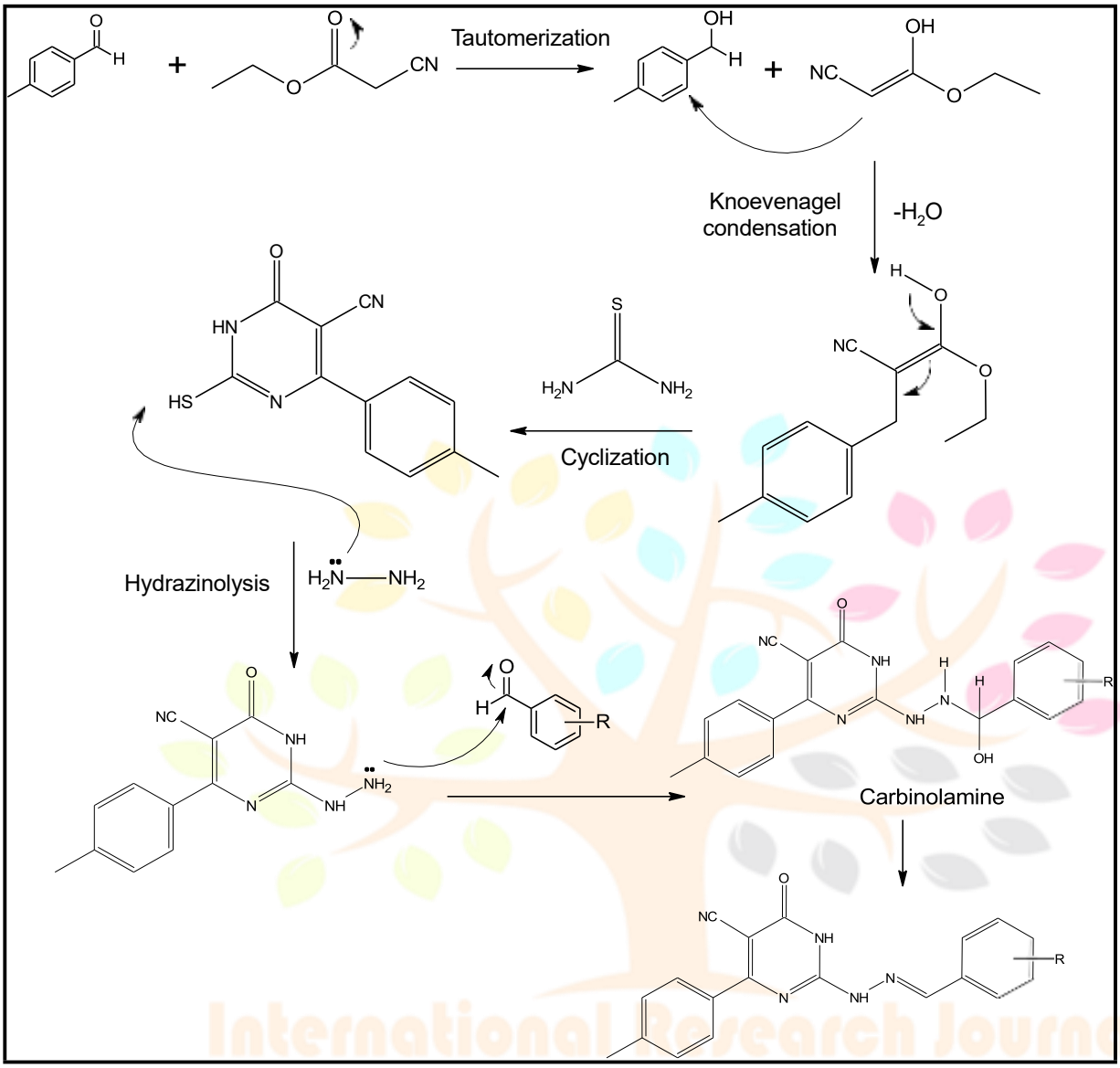
1. To synthesize pyrimidine derivatives by both, the conventional and microwave irradiation methods.
2. To purify the synthesized compounds by recrystallization.
3. To characterize the compounds using FT-IR, MS, NMR spectroscopic techniques.
4. To evaluate the synthesized compounds for antimicrobial activity.
5. This method is preffered over traditional method because it is faster, more efficient.

REACTION



Scheme 5.1. (a) Reaction summary for synthesis of Pyrimidine Schiff base derivatives

Mechanism of action:



Scheme 5.1. (b) Mechanism of Action for synthesis of Pyrimidine Schiff base derivatives

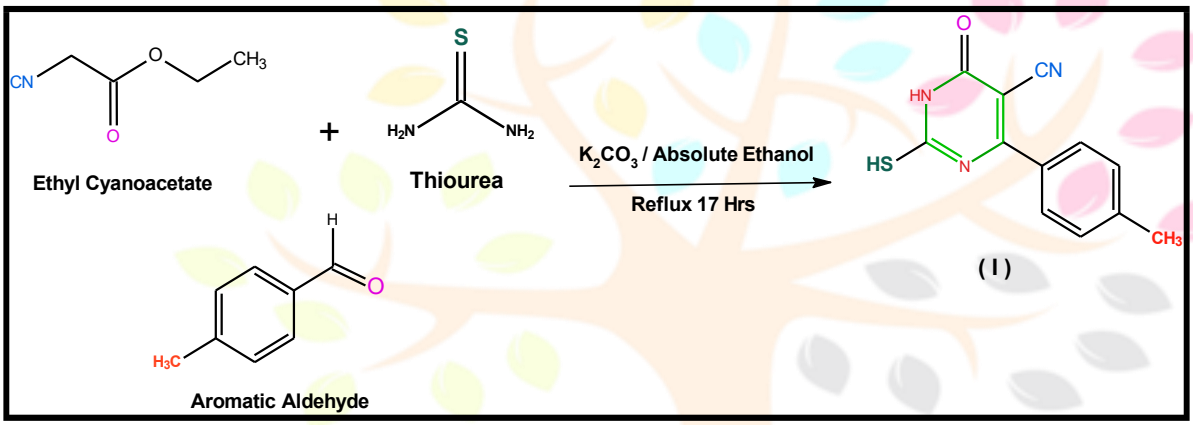
Procedure

Step I: Synthesis of 2-mercapto-6-(p-tolyl)-4-oxo-1,4-dihydropyrimidine-5-carbonitrile

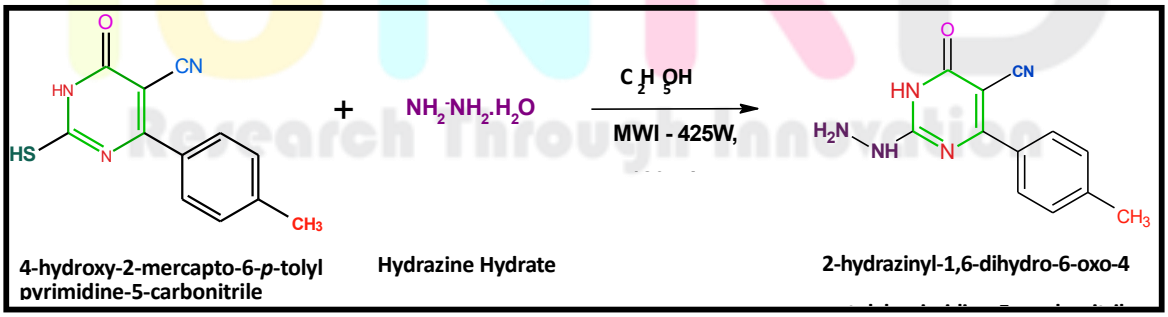
Intermediate I was synthesized via one pot cyclocondensation reaction, in which equimolar quantities of ethyl cyanoacetate, aromatic aldehydes and thiourea allowed to react in absolute ethanol in presence of anhydrous potassium carbonate reflux for 17 hrs to obtain 2-mercapto-6-(p-tolyl)-4-oxo-1, 4-dihydropyrimidine-5-carbonitrile (I). The reaction was monitored using ethyl acetate and n-hexane in a ratio of 1:4 as mobile phase on a TLC plate. The resulting solution was dissolved in hot water and glacial acetic acid was added dropwise and kept overnight for precipitate to form. The formed precipitated solid was washed with cold water and vacuum filtered, dried, and recrystallized with a mixture of ethanol-acetone. On drying, the melting point of the compound was recorded. The completion of the reaction was monitored by TLC.(5)

Scheme 5.2 Synthesis of 2-mercapto-6-(p-tolyl)-4-oxo-1, 4-dihydropyrimidine-5-carbonitrile

Step II: Synthesis of 6-(p-tolyl)-2-hydrazino-4-oxo-1, 4-dihydropyrimidine-5-carbonitrile (Intermediate II)



mol 4-hydroxy-2-mercapto-6-*p*-tolylpyrimidine-5-carbonitrile (Intermediate I) was reacted with 0.02 mol hydrazine hydrate (99%) and absolute ethanol (50 mL) was refluxed under microwave irradiation at a power of 50% and 450W for 120 mins to obtain 0.02 intermediate II. The formed solid was filtered on Buchner funnel, air dried and a mixture of ethanol-acetone were used to recrystallize the compound. Reaction progress was verified with TLC in a mobile phase of ethyl acetate and n- hexane (1:4). Melting point was noted down.(8)

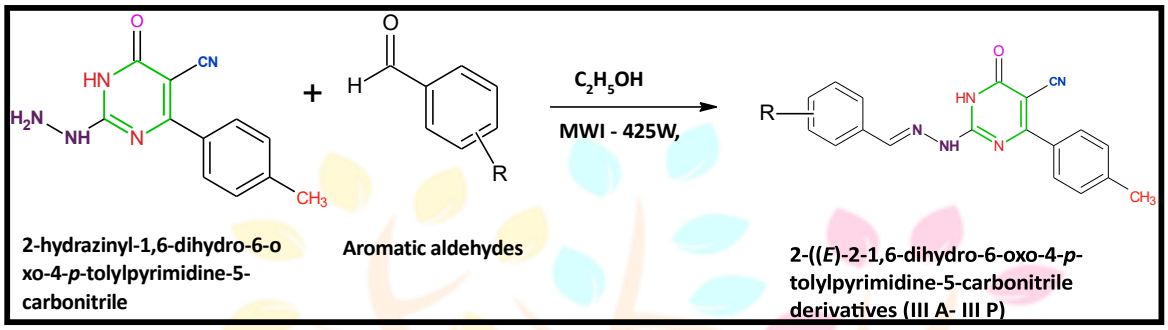


Scheme 5.3: Synthesis of 6-(p-tolyl)-2-hydrazino-4-oxo-1, 4 dihydropyrimidine-5-carbonitrile

Step III: (E)-2-[(1-(Substituted-phenyl)et hylidene)hydrazino]-6-(p-tolyl)-4-oxo-1,4-dihydropyrimidine-5-carbonitrile derivatives

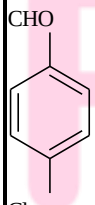
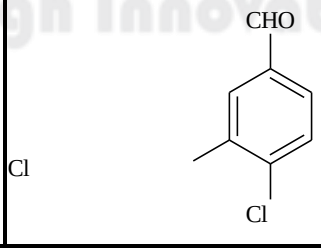
0.01 mol 2-hydrazinyl-1,6-dihydro-6-oxo-4-*p*-tolylpyrimidine-5- carbonitrile and 0.01 mol substituted aromatic aldehydes was refluxed in ethanol under microwave irradiation at a power of 50% and 450W for about 90 mins to 3 hours. Resulting solution was filtered, dried, and recrystallized with a mixture of ethanol-acetone. TLC mobile phases ethyl acetate and n-hexane in ratio 1:4 were used to determine completeness of the reaction and melting point was documented.(11)

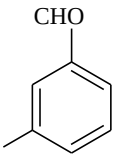
Scheme 5.4: Synthesis of (E)-2-[(1-(Substituted-phenyl)et hylidene)hydrazino]-6-(p-tolyl)-4-oxo-1,4-dihydropyrimidine-5-c arbonitrile derivatives



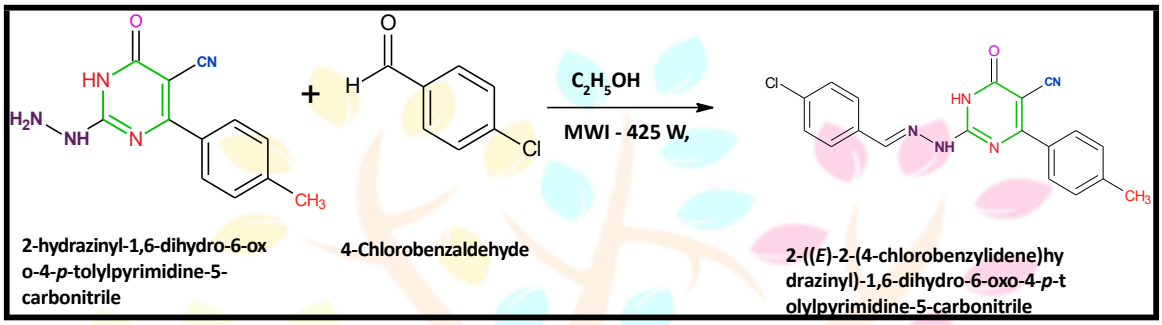
Numerous aromatic aldehydes to accomplish pyrimidine bases were casted-off as given in the table a below:

Table a. List of aromatic aldehydes employed in the reaction

Compounds	Aldehydes Used	
	Name	Structure
III-A	p-Chloro benzaldehyde	
III-B	3,4-Dichlorobenzalddehyde	

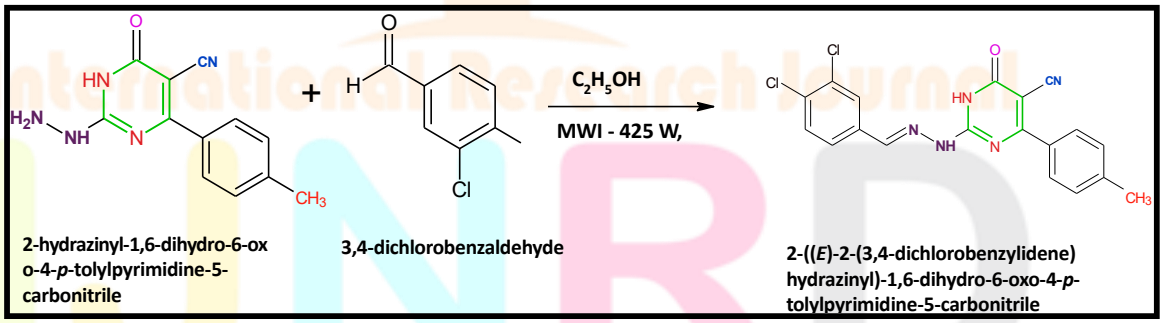
III-C	3-Nitrobenzaldehyde	**O2N** 

Step III-A:



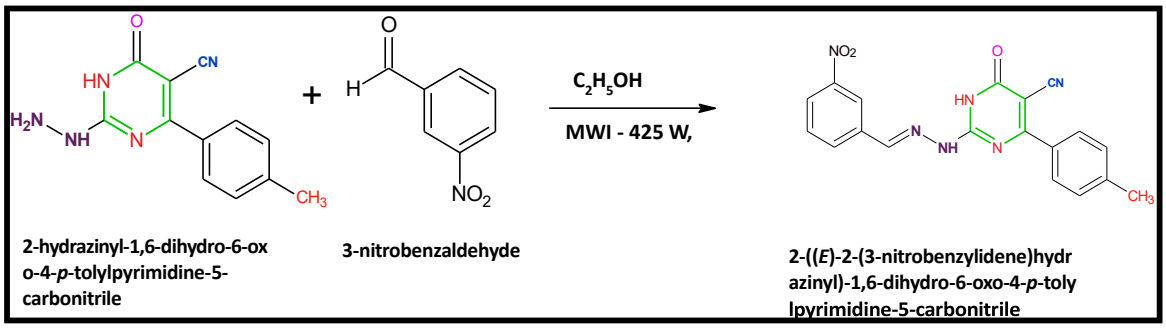
5.4.1. Synthesis of 2-((*E*)-2-(4-chlorobenzylidene)hydrazinyl)-1,6- dihydro-6-oxo-4-*p*-tolylpyrimidine-5-carbonitrile

Step III-B:



5.4.1. Synthesis of 2-((*E*)-2-(3,4-dichlorobenzylidene)hydrazinyl)-1,6- dihydro-6-oxo-4-*p*-tolylpyrimidine-5-carbonitrile

Step III-C:



5.4.1. Synthesis of 2-((*E*)-2-(3-nitrobenzylidene)hydrazinyl)-1,6-dihydro-6- oxo-4-*p*-tolylpyrimidine-5-carbonitrile

Microwave Assisted Synthesis: Microwave irradiated synthesis has not only grabbed the research interest, but has also occupied an integral portion of synthetic chemistry. Hence, we optimized the reaction conditions of the designed scheme conventionally and with microwave thereafter. The reaction conditions for synthesis step-II and Step-III of the reaction scheme were kept consistentusing the microwave method. Initially the reaction was run at 340W (40%), which required more time for reaction completion while the same reaction at 425 (50%) power consumed lesser time and so, 50% power was chosen for synthesis. A total of 16 derivatives were synthesized and processed through qualitative analysis and antimicrobial evaluation

ANALYTICAL TECHNIQUES

There are so many analytical techniques for determination, detection, and characterization of unknown compounds. Some of the analytical techniques implemented in this study were Thin Layer Chromatography (TLC), Melting Point (M.P), Fourier Transform Infra-Red Spectroscopy (FTIR), Proton Nuclear Magnetic Resonance (1H NMR), Carbon-13 Nuclear Magnetic Resonance (13C NMR), Mass Spectroscopy.

1.Thin Layer Chromatography (TLC):

In organic chemistry, Thin Layer Chromatography (TLC) is a technique for analysing mixtures of organic compounds and tracking reaction completion. The progress of reactions was assessed with Merck pre-coated silica gel 60 F254 obtained from Merck, Specialities Ltd., Mumbai. The materials used during TLC were:

1. Spotting- TLC spotting done by one end closed glass capillary tubes.
2. Development- Ascending elution method employed for the development of plates.
3. Mobile phase for development involved altered ratio mixtures of ethyl acetate and n-hexane.
4. Visualization- Method: non-destructive UV lamp (long-waved; 365nm) Instrument: UV cabinet

Method for analysis:

Mobile phase was first prepared in appropriate ratios and the TLC chamber was lid for saturation (Chamber saturation). Simultaneously, while waiting for the chamber to get saturated, a small quantity of reaction mixture/product was diluted with ethanol in a fusion tube. A TLC plate was taken and 3 components namely ethyl cyanoacetate (x1), aromatic aldehyde (x2) used and product (x3) were spotted with one end closed capillary tube. Plate was developed by placing it into a saturated chamber, allowed to run up to a required distance, plates were removed and viewed in a UV cabinet (long UV-365nm). The spots were marked and distance travelled by the spots (x1, x2, x3) as well as by the mobile phase (y) was measured.(29)

2.Melting Point (MP):

The melting point (MP) of a compound is the temperature at which it transitions from a solid to a liquid at atmospheric pressure. It is a key physical property used to characterize and identify pure substances. A narrow melting point range (typically within 1–2 °C) indicates high purity, while a broader range or deviation from the known melting point suggests impurities or the presence of a mixture.(20)

Procedure

1. **Sample Preparation:**

Crush the dry compound into a fine powder using a mortar and pestle

- Fill a clean, dry capillary tube with the sample to a height of 2–3 mm. Tap gently to ensure the sample is compacted evenly at the bottom.

2. **Initial Rough Melting Point:**

- Insert the capillary tube into the melting point apparatus.
- Heat the sample gradually (~5–10 °C/min) and observe the temperature range at which the compound starts and finishes melting.
- This provides an approximate melting point.

3. **Accurate Determination:**

- Allow the apparatus to cool.
- Insert a new capillary tube with the same sample.
- Heat the sample slowly (~1–2 °C/min) near the expected melting point.
- Record the temperature at which the first sign of liquid is observed (onset of melting) and the temperature at which the sample is fully liquefied (end point).

4. **Repeatability:**

- Repeat the measurement 2–3 times to confirm consistency and accuracy.

Table C. Molecular properties of compounds (MF, FW, Rf, MP) with yield

Synthesized Compounds	Molecular Formula	Formula Weight (g/mol)	Rf Values	Melting point(°C)	Yield (%)
III-A	$C_{19}H_{14}ClN_5O$	363.80	0.8	123	70.40
III-B	$C_{19}H_{13}Cl_2N_5O$	398.24	0.6	127	58.28
III-C	$C_{19}H_{14}N_6O_3$	374.35	0.73	135	67.27

3.Fourier Transform Infra-Red Spectroscopy (FTIR):

Compound III-A

2-((*E*)-2-(4-chlorobenzylidene)hydrazinyl)-1,6-dihydro-6-oxo-4-*p*- tolylpyrimidine-5-carbonitrile

FTIR

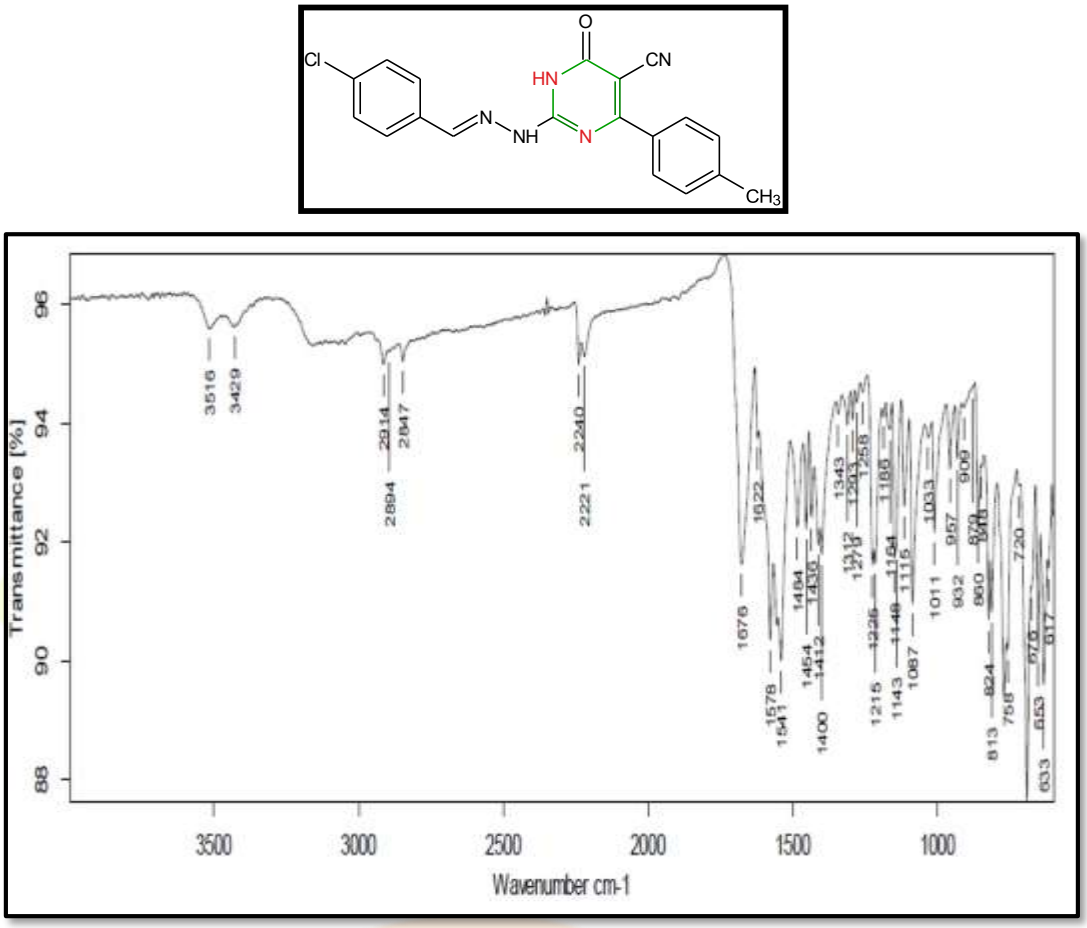


Fig (a) IR spectra for compound III-A

Table (a) IR interpretation for compound III-A

Functional Groups	Actual Frequencies	Observed Frequencies
N-H	3500-3100	3516
C-H Stretch (aromatic)	3000-2850	2914
C≡N	2260-2240	2240
C=O stretch	1725-1705	1676
C=N stretch	1690-1640	1578

C=C (alkene)	1680-1600	1622
C=C (aromatic)	1600-1475	1541
-CH_3 bend	1450-1375	1454
-CH_2 bend	1465	1484
C-N stretch	1350-1000	1400
=C-H out of plane bend	900-690	957
C-Cl	667	758

Compound III-B

2-((*E*)-2-(3,4-dichlorobenzylidene)hydrazinyl)-1,6-dihydro-6-oxo-4-*p*- tolylpyrimidine-5-carbonitrile

FTIR

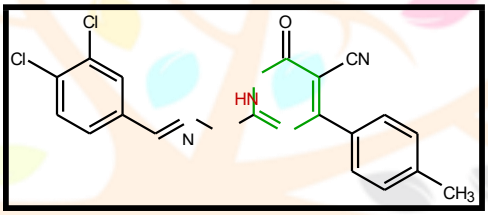
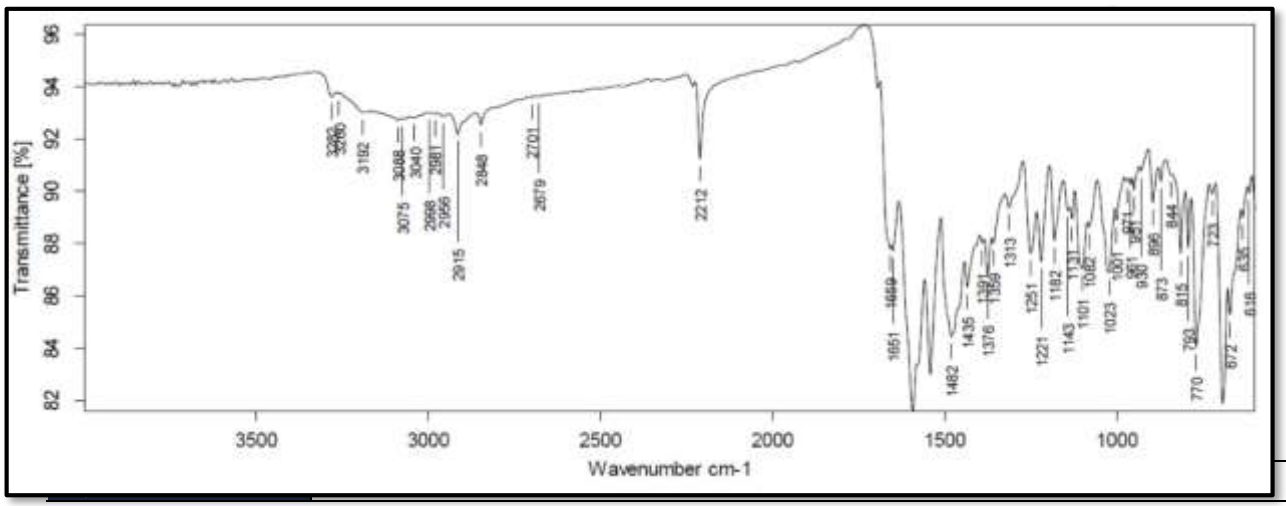


Fig (b). IR spectra for compound III-C

Table (b). IR interpretation for compound III-C

Functional Groups	Actual Frequencies	Observed Frequencies
N-H	3500-3100	3281
C-H Stretch (aromatic)	3000-2850	2915
C≡N	2260-2240	2212
C=O stretch	1725-1705	1659
C=N stretch	1690-1640	1651
C=C (alkene)	1680-1600	1593
C=C (aromatic)	1600-1475	1482
-CH_3 bend	1450-1375	1435



-CH_2 bend	1465	1391
C-N stretch	1350-1000	1251
=C-H out of plane bend	900-690	896
C-Cl	667	672

Compound III-C

2-((*E*)-2-(3-nitrobenzylidene)hydrazinyl)-1,6-dihydro-6-oxo-4-*p*- tolylpyrimidine-5 carbonitrile

FTIR

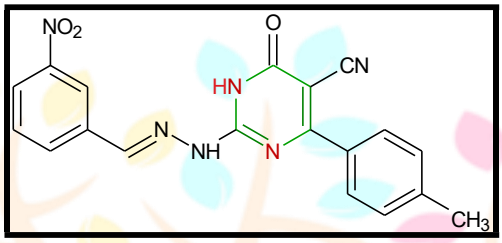
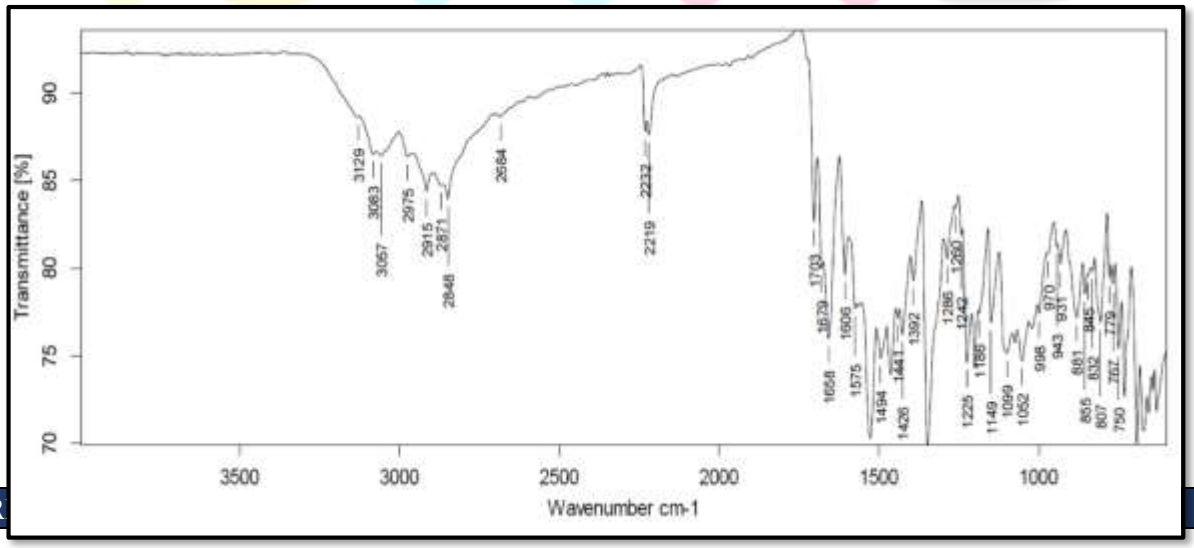


Fig (c). IR Spectra for compound III-E

Table (c) IR interpretation for compound IIIE

Functional Groups	Actual Frequencies	Observed Frequencies
N-H	3500-3100	3057
C-H Stretch (aromatic)	3000-2850	2915
C≡N	2260-2240	2219
C=O stretch	1725-1705	1703
C=N stretch	1690-1640	1679
C=C (alkene)	1680-1600	1658
C=C (aromatic)	1600-1475	1564
-CH_3 bend	1450-1375	1463
-CH_2 bend	1465	1426
C-N stretch	1350-1000	1225
=C-H out of plane bend	900-690	881



C-Cl	667	672

Nuclear Magnetic Resonance (NMR) Spectroscopy:

This is a well-known scientific technique that involves monitoring the interaction of radiofrequency (Rf) electromagnetic radiations with the nuclei of molecules placed in a strong magnetic field to identify and analyse their structure.

The three synthesised compounds were analysed for both proton (1H) NMR spectroscopy

Proton (1H) NMR: 3 compounds were detected using 1H NMR spectroscopic method, dissolved in deuterated dimethyl sulfoxide (DMSO-d_6).

1H NMR (III-A)

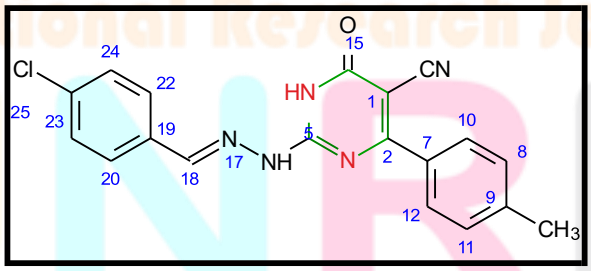
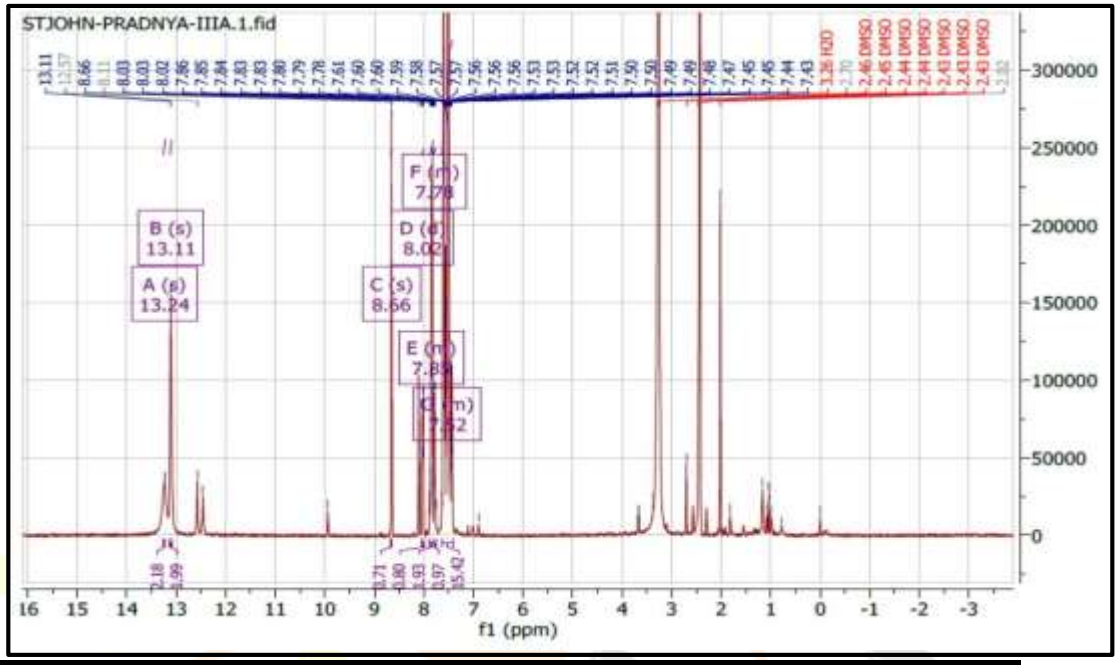


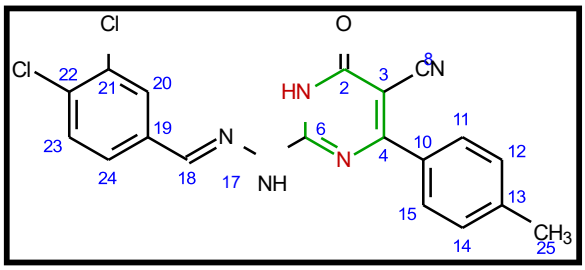
Fig (a) 1H NMR spectra for compound III-A

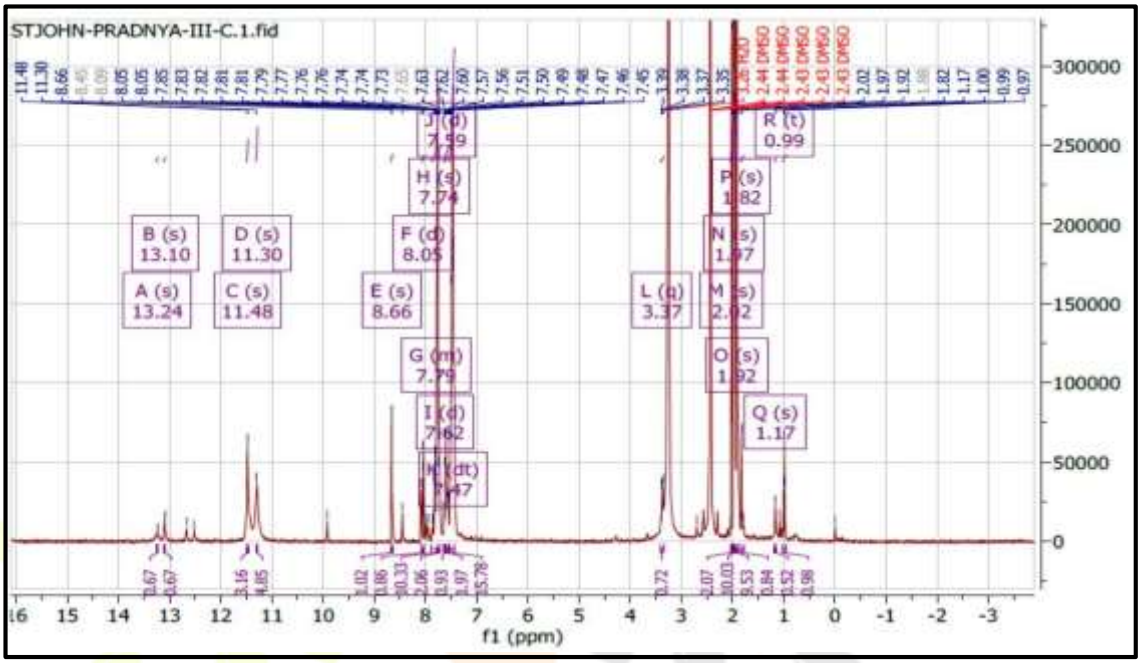
Table (a) 1H NMR interpretation for compound III-A



Sr No	δ ppm	Splitting Type	No. of Protons	Protons Involved
1	7.52	Doublet	2H	H10, H12
2	7.85	Doublet	2H	H08, H11
3	8.02	Singlet	1H	H18
4	7.78	Doublet	2H	H20, H22

1H NMR SPECTRA (III-B)



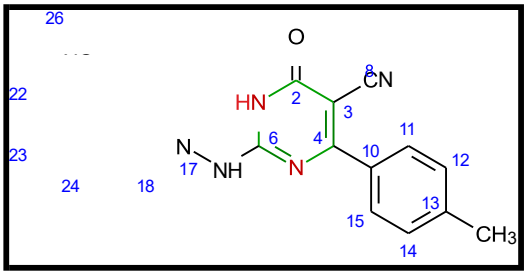


Fig(b). 1H NMR spectra for compound III-B

Table (b). 1H NMR interpretation for compound III-B

Sr No.	δ ppm	Splitting Type	No. of Protons	Protons Involved
1	7.47	Doublet	2H	H11, H15
2	7.74	Doublet	2H	H12, H14
3	7.62	Doublet	2H	H20, H24
4	7.59	Doublet	2H	H23, H26
5	2.02	Singlet	1H	H25
6	8.05	Singlet	1H	H1
7	8.66	Singlet	1H	H18

1H NMR SPECTRA (III-C)



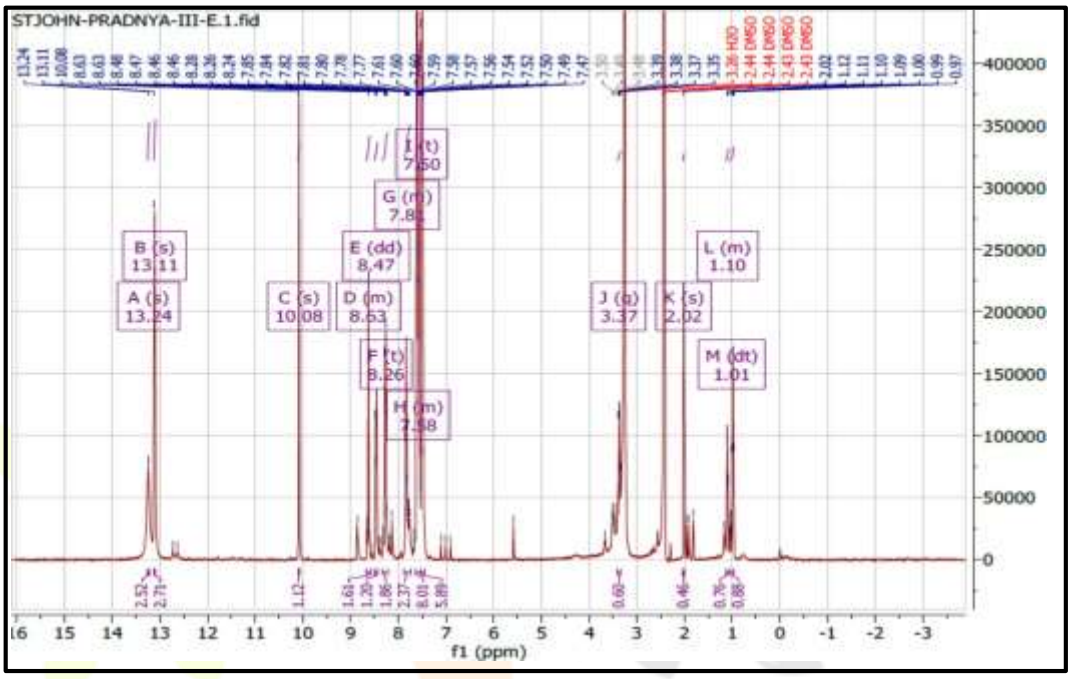


Fig (c). 1H NMR spectra for compound III-C

Table (c). 1H NMR interpretation for compound III-C

Sr No	δ ppm	Splitting Type	No. of Protons	Protons Involved
1	7.50	Doublet	2H	H12, H14
2	7.58	Doublet	2H	H11, H15
3	7.81	Singlet	1H	H23
4	8.47	Doublet	2H	H1, H24
5	8.53	Singlet	1H	H18
6	2.02	Singlet	1H	H16

Mass Spectroscopy:

It calculates the compounds mass to charge (m/z) ratios. The heights of the peaks in a mass spectra indicate the relative abundance of the various components in the sample, while the peaks themselves reveal distinct m/z in the sample.

Mass spectra III-A

Molecular formula: $C_{19}H_{14}ClN_5O$

Formula weight: 363.80036 g/mol

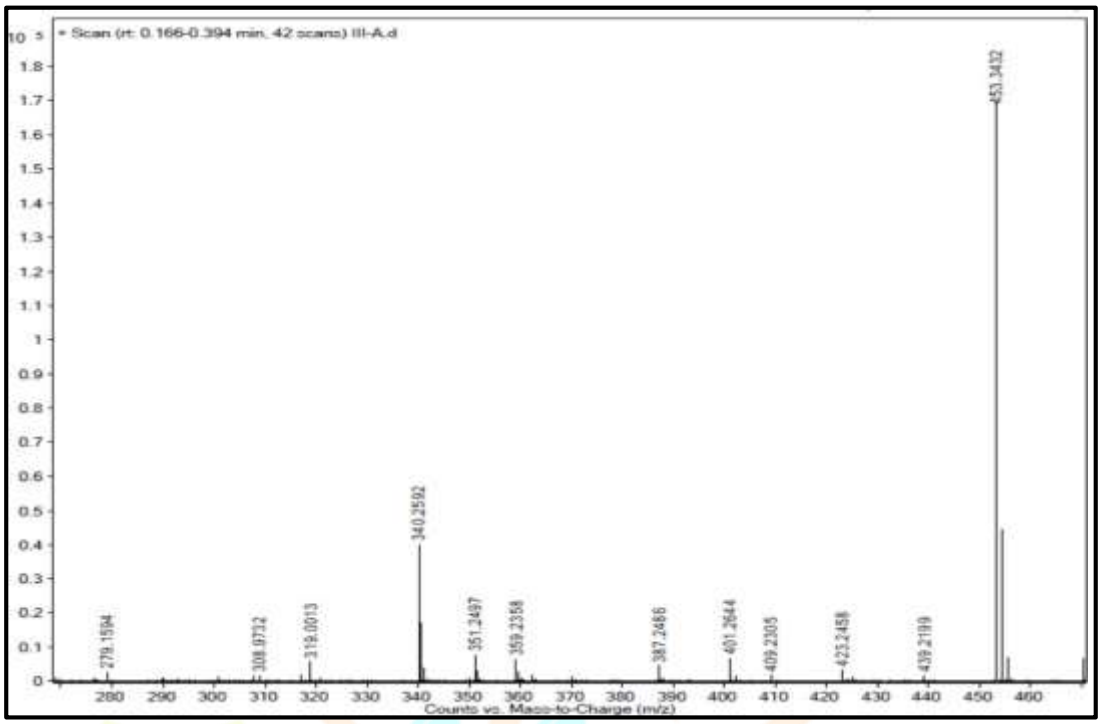


Fig (a) Mass spectra for compound III-A m/z: 359.23 Da [M-]

Mass spectra (III-B)

Molecular Formula: $C_{19}H_{13}Cl_2N_5O$

Formula Weight: 398.24542 g/mol

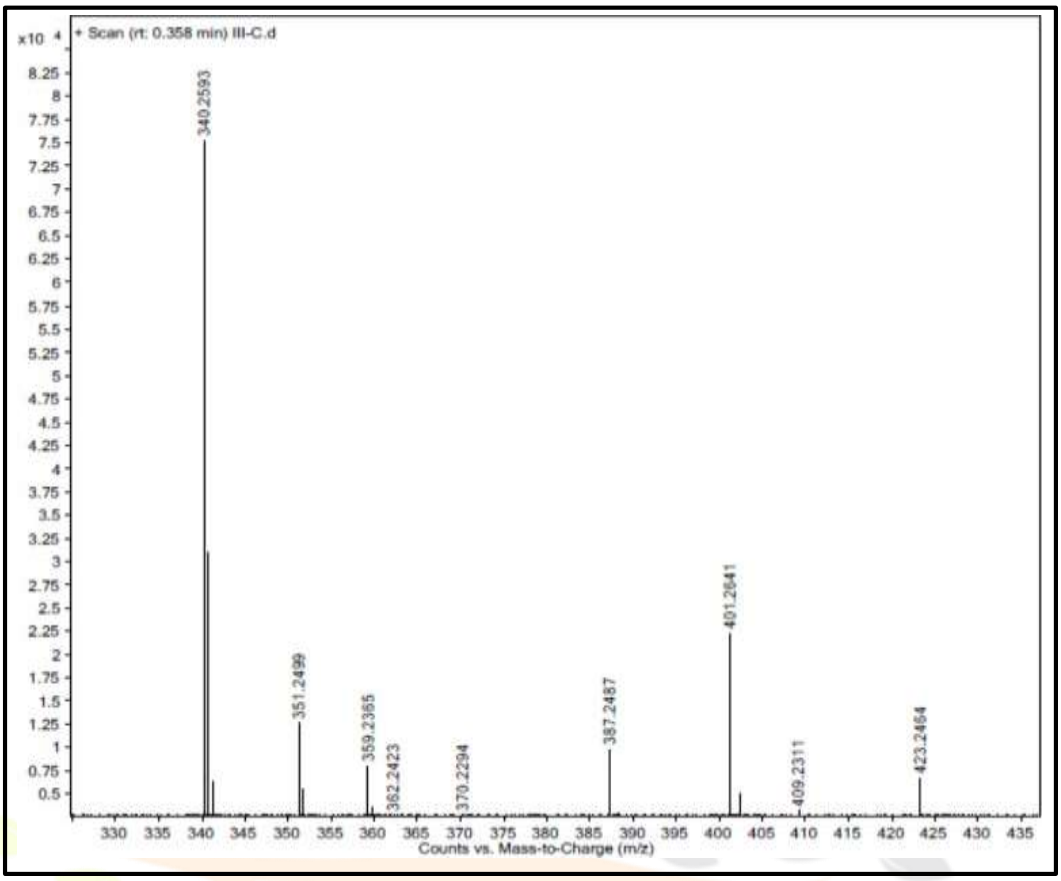


Fig (b). Mass spectra for compound III-B

m/z: 401.26 Da [M+]

Mass spectra (III-C)

Molecular Formula: $C_{19}H_{14}N_6O_3$

Formula Weight: 374.3523114 g/mol

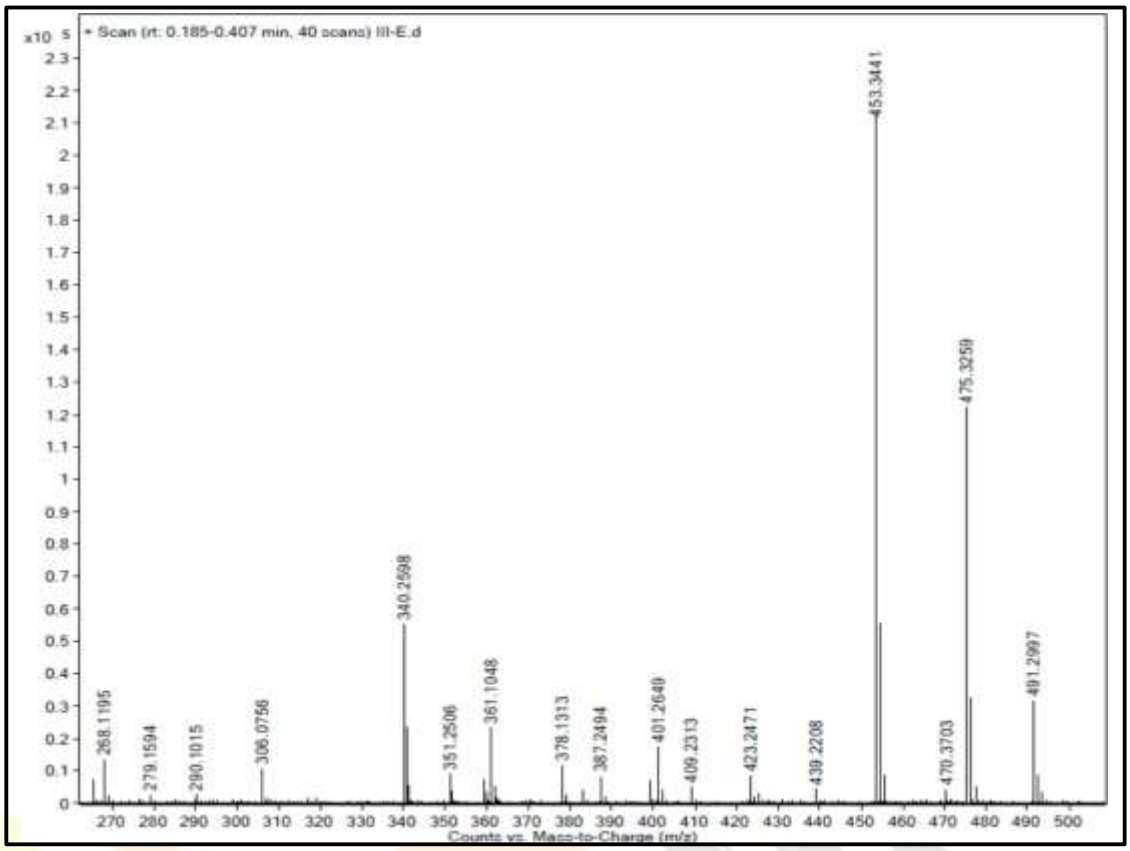


Fig (c). Mass spectra for compound III-C

m/z: 378.13 Da [M+]

ANTIMICROBIAL EVALUATION

The purpose for synthesis of such compounds was to identify the biological activity of compounds. More specifically gaging their antimicrobial activity remained the prime intention. Structure activity correlation was the outcome of this antibacterial activity. Study of change in the activity with change of substituents forms the paradigm of this project thus enabling a systematic understanding of the synthesized derivatives.

Requirements:

Apparatus: Volumetric flask (10 mL and 500 mL), test tubes, micro pipettes**,** petri plates,paper disks (5mm).
Chemicals: Ciprofloxacin tablet (Cifran® 250), Synthesized compounds, dimethyl sulphoxide (DMSO), nutrient agar medium, distilled water
Microorganisms:

Gram positive organisms: *Staphylococcus aureus* (SA)

Gram negative organisms: *Escherichia coli* (EC)

Procedure:

Preparation of test organisms:

Test organisms of Microbial type cell cultures (MTCC) strains were procured from CSIR- Institute of Microbial Technology. Organisms were grown in nutrient broth medium to be used for antimicrobial evaluation. Fresh cultures were used for this purpose.

Preparation of standard solution (Ciprofloxacin Tablet): Ciprofloxacin incorporated as standard in estimation of antimicrobial activity, the drug inform of tablet was utilized under the study, the brand name being Cifran 250 mg. Firstly,the average of 5 weighed tablets were recorded. Triturated tablets equivalent to 100 mg added to a volumetric flask (100mL), followed by addition of distilled water (necessary tosolubilise the powder), sonicated for few minutes, and further distilled water poured to fill it to the mark to produce 1mg/mL of homogenous solution.

Weight of 5 tablets = 1909 mg (1.909 gm)

Average weight of tablet = 381.8 mg (0.381 gm381.8 mg contains 250 mg of ciprofloxacin **contain 100 mg of Ciprofloxacin**

API

$\therefore x = \frac{100 \times 381.8}{250} = 152.72$ mg

152.72 mg powder solubilised in 100 mL distilled water to produce 1000 µg/mL (stocksolution

Now, 0.25, 0.5, 1 & 2 mL of above stock solution individually with 100 mL

distilled waterresulted in 25, 50, 100 & 200 µg/mL solution respectively. Thus, a prepared 100 µg/mL solution was utilized as a standard solution for antimicrobialactivity evaluation.

Preparation of test solution:

Stock solution- 10 mg of synthesized analogues were weighed and dissolved in 10 mLDMSO to produce 1000 µg/mL stock solution.

Test dilutions- 0.25, 0.5, 1, 2 mL stock solutions were diluted up to 10 mL with DMSO to give 25, 50, 100 and 200 µg/mL solutions respectively.

Media preparation:

Suspend 40 grams of nutrient agar medium powder in 1000mL distilled water. Heat toboiling to dissolve the medium completely. Sterilize by autoclaving at 15 lbs pressure (121°C) for 15 minutes. After allowing the mixture

to cool, the microbiological assay procedurewas conducted immediately

Method for assessment: The **Disk Diffusion Assay method** was applied to assess the synthesised derivatives. Sterilized plates were serially organised and labelled with the compound number and organisms. 0.1mL broth cultures were used to inoculate plates. After that, about 20mL of sterlised agar was poured onto plates and allowed to set for quite a while. Disks were soaked in the standard and test solutions and dried at the same time. After the plates had solidified, the plates were impregnated with the soaked discs. The plates were incubated for 24 hours at 37°C. The area around the discs where no bacteria were found (Zone of Inhibition) was measured in millimetres on petri plates (mm). These ZOI values were used to calculate the Minimum Inhibitory Concentration (MIC) in µg/mL.

RESULT

For the synthesis of anticipated compounds, first step synthesized through conventional and step two and three synthesized via microwave synthesizer. Ethyl cyanoacetate, Potassium carbonate anhydrous, Thiourea and 4-Methyl Benzaldehyde were the parent raw materials incorporated for synthesis which successively proceeded through three steps utilizing appropriate solvents and reagents to finally yield 2-((E)-2-1,6-dihydro-6-oxo-4-p- tolylpyrimidine-5-carbonitrile derivatives. The synthesized compounds were verified by their Rf values and melting points and were subjected to weighing for their yield.

DISCUSSION

Pyrimidine-based derivatives have emerged as a critical class of heterocyclic compounds with extensive pharmaceutical relevance. The pyrimidine ring, a fundamental component of nucleic acids, provides a versatile scaffold for the development of bioactive molecules. Advances in synthetic strategies have enabled the efficient and selective modification of the pyrimidine core, allowing researchers to fine-tune their physicochemical and biological properties.

Pharmacologically, pyrimidine derivatives exhibit a wide spectrum of activities, including anticancer, antiviral, antibacterial, antifungal, anti-inflammatory, and CNS-modulating effects. These activities are attributed to their ability to interact with key biological targets such as enzymes (kinases, polymerases), nucleic acids, and receptors. For example, compounds like 5-fluorouracil (anticancer), zidovudine (antiviral), and pyrimethamine (antimalarial) underscore the clinical significance of this scaffold.

CONCLUSION

- We aimed synthesize pyrimidine containing leads as potential antimicrobial agents.
- Literature highlighted pharmacological importance of Pyrimidine bases and so we selected this active moiety to progress for the study.
- Synthesized derivatives were effectively established through qualitative analytical tools like Thin Layer Chromatography and Melting Point determination. Detailed characteristic study and data interpretation was achieved with advanced spectroscopic methods like FTIR, 1H NMR, 13C NMR and Mass Spectroscopy
- This concludes that the project accomplished its stated objectives of synthesizing, and evaluating the potential of compounds as an antimicrobial agent.

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