IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

SYNTHESIS OF 2,4,5 TRIPHENYL IMIDAZOLE

1Mr.Rohit Keshav Dimote, 2Asst.Prof.Khandre Rajeshree

1Pharmacy, 2Pharmacy

1Prathibhatai Pawar college of Pharmacy,

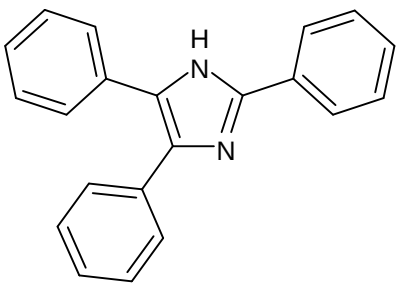
2Prathibhatai Pawar college of Pharmacy

- **ABSTRACT:-**

On the basis of various literature survey, imidazole derivatives show various activity such as antimicrobial, anti-inflammatory, analgesic, antitubercular, anticancer etc. The possible improvements in the activity can be further achieved by slight modifications in the substituents on the basic imidazole nucleus. Having structural similarity with histidine imidazole compound can bind with protein molecules with ease compared to some other heterocyclic moieties. Thus, imidazole offers better pharmacodynamic characteristics. Furthermore, some imidazole drugs, at high concentrations, could exert direct inhibitory effects on membranes, without interference with sterols and sterol esters. Various recent new drugs developments in imidazole derivatives show better effect and less toxicity. Prompted by the broad-spectrum activities of 2, 4, 5- triphenylimidazole derivatives, it was decided to synthesize various 2, 4, 5-triphenyl-1-substituted imidazole's and to evaluate them for their pharmacological activities.

- **INTRODUCTION:-**

TRIPHENYL IMIDAZOLE



Imidazole's are probably the most well-known heterocycle which is common and important feature of a variety of natural products and medicinal agents.

The compound$C_{21}H_{16}N_2$, has been known since 1877. Although the crystal structure of 36 derivatives of lophine are known, the structure of parent compound has remained unknown until now.

The three phenyl rings bonded to the imidazole core are not coplanar with the latter, with dihedral angles of 21.4 (3), 24.7 (3), and 39.0 (3) °, respectively, between the phenyl ring planes in the 2-, 4- and 5-positions of the imidazole ring. The molecules are packed in layers running perpendicular to the *b* axis. There are acceptor and donor atoms for hydrogen bonds.

The synthesis of novel 2,4,5-triphenylimidazole derivatives seems to be main focus of the medicinal research because compounds containing triphenyl imidazole moiety provides a number of needful biological activities such as analgesic and anti-inflammatory activities

(Shalini *et al.*, 2011; Achar *et al.*, 2010). Anti-inflammatory activity (Yashoda *et al*., 2009). The substitution at C-2 benzene nucleus with benzyl, benzoyl, para-amino benzoyl antifungal activity (Yadav *et al*., 2011). The 2,4,5-triphenyl nucleus had been synthesized by microwave technique as well (Pandit *et al*., 2011). The trimethoxy benzene nucleus at the 2 position of imidazole ring in anti-inflammatory and antifungal activities (Umarani *et al.*, 2011). Addition of thio group in 2,4,5-triphenylimidazole in increased activity (El Ashry *et al*., 2007).

Azole ring in place of abstractable hydrogen in 2,4,5-triphenylimidazole ring potent antibacterial and anti-inflammatory activity (Amir *et al*., 2011).

On the basis of various literature surveys Imidazole derivatives shows various pharmacological activities:

Anti-fungal and Anti-bacterial activity

Anti-inflammatory activity and analgesic activity

Anti-tubercular activity

Anti-depressant activity

Anti-cancer activity

Anti-viral activity

Antileishmanial activity

Anti-arthritic activity

Anti-angiogenesis

In this present study 1-H substituted 2,4,5 triphenyl imidazole derivative is designed, synthesized and their biological activities were screened.

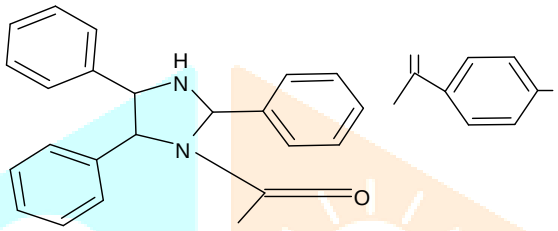
Biological significance of imidazole: Imidazole is incorporated into many important biological molecules. The most important is the amino acid histidine, which has an

imidazole side chain. Histidine is present in many proteins and enzymes play a vital role in the structure and binding functions of haemoglobin. Histidine can be decarboxylated to histamine, which is also a common biological compound. It is a component of the toxin that causes urticaria, i.e., allergic.

- **LITERATURE REVIEW:-**

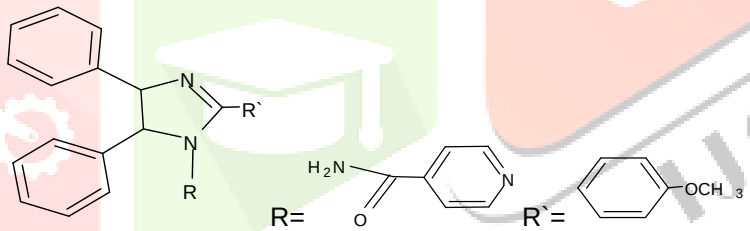
1) Burungale and bhitre et al., (2013),

Synthesis of 2,4,5triphenyl imidazole derivatives and biological evaluation for them antibacterial and anti-inflammatory activity.



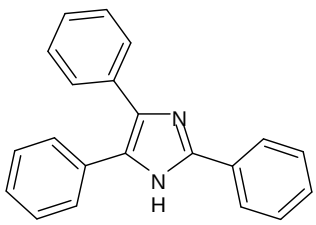
2) Sharma *et al.*, (2013),

Microwave irradiated synthesis of some substituted imidazole derivatives as potential antibacterial and anticancer agents.



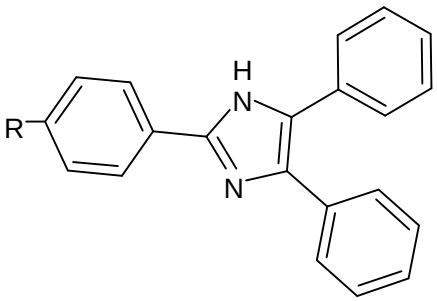
3) Burungaleswati *et al.*, (2013),

Synthesis of 2,4,5triphenyl imidazole derivatives and biological evaluation for their analgesic and anti-inflammatory activity.



4) Kumar Vikrant et al., (2012),

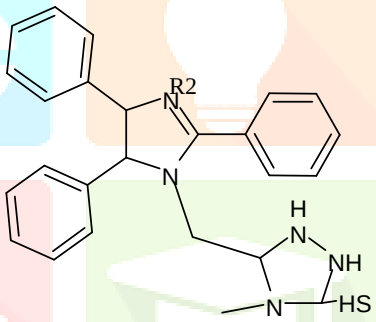
A robust and reliable one pot synthetic method has been developed for 2,4,5 tri substituted imidazole the synthetic sequence via, a multi – component condensation catalyzed by p-toluene sulfonic acid, provides good isolated yields under mild conditions.



R=H,CH3,OCH3,Cl

5) Rajeev Kharb *et al*., (2012),

Synthesis and spectral characterization and anthelmintic evaluation of some novel imidazole bearing triazole derivatives.



R2=C6H5

- **AIM AND OBJECTIVE :-**

AIM OF PRESENT STUDY:

Triphenylimdazole is a best nucleus and biologically active molecule. Now a day this is interesting research nucleus of substituted derivative.

The aim of the present study was to obtain triphenyl imidazole as biologically effective agent with good therapeutic values and minimum toxic levels.

Past few years most of the research fellowship has done the project in triphenylimidazole by the substitution of primary amine in the position of 1H group in imidazole. But I like to alter the simple modification in the synthesis for evaluate the anti-arthritic anti – oxidant, anti-angiogenesis and anti-microbial activities.

Step 1: Here I decided to substitute the different aldehyde in the reaction of benzil and ammonium acetate.

Step 2: Here I decided to substitute the different amine in the reaction of triphenyl imidazole and formaldehyde.

OBJECTIVE OF PRESENT WORK:

Synthesis:

Step I:

Synthesis of tri phenyl imidazole derivative.

Step II:

Synthesis of 2,4,5triphenyl -1H-imidazole derivatives (compound A1- A5).

Synthesis of 5-(chlorophenyl)-2,4diphenyl -1H-imidazole derivatives (compound A6 –A1).

Software used:

- Chemskech
- Chemdoodle Molinspiration

Spectral studies:

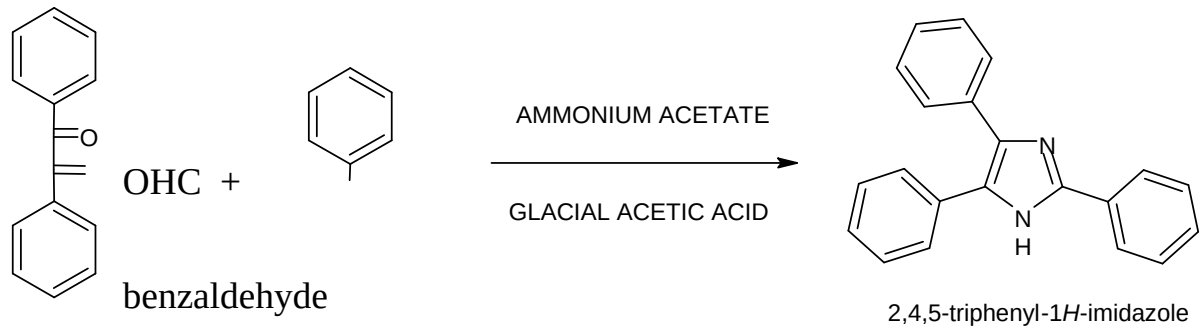
- Infrared spectroscopy
- Nuclear Magnetic Resonance spectroscopy
- Mass spectroscopy
- Biological evaluation:
- In vitro Antimicrobial Activity
- In vitro Antioxidant Activity

In vitro Antiarthritic Activity

In vivo Antiangiogenesis Activity.

- **SCHEME OF REACTION :-**

STEP –I PREPARATION OF2,4,5 TRIPHENYL -1H- IMIDAZOLE

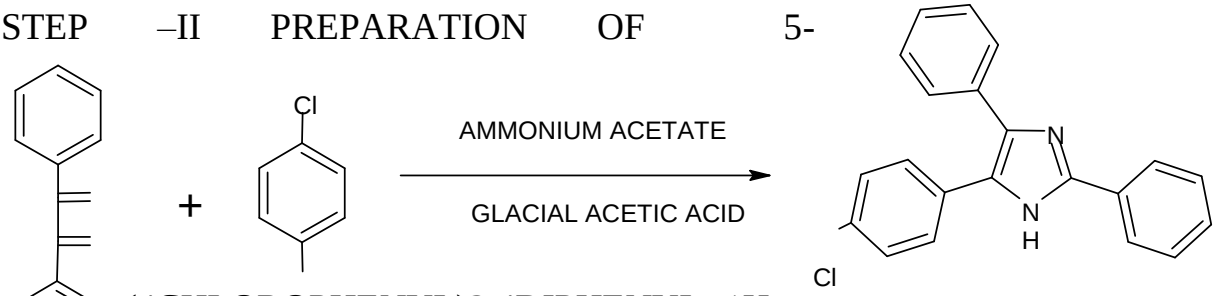


benzaldehyde

2,4,5-triphenyl-1*H*-imidazole

1,2-diphenylethane-1,2-dione

STEP –II PREPARATION OF 5-



(4CHLOROPHENYL)2,4DIPHENYL- 1H-IMIDAZOLE

O

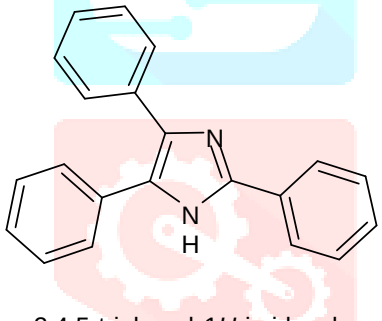
O

CHO

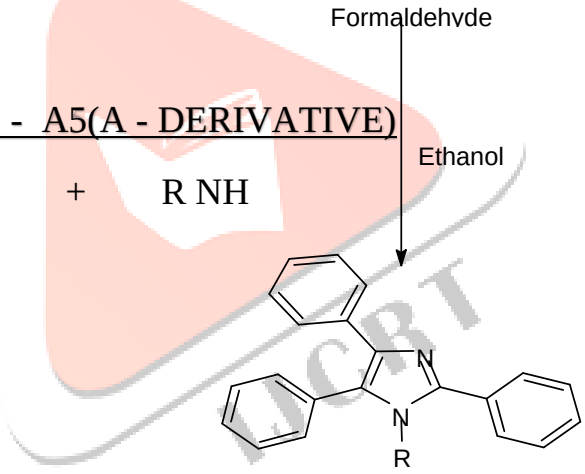
4-chlorobenzaldehyde 5-(4-chlorophenyl)-2,4-diphenyl-1*H*-imidazole

STEP –III

PREPARATION OF 1H- SUBSTITUTED TRIPHENYL IMIDAZOLE DERIVATIVES



2,4,5-triphenyl-1*H*-imidazole



COMPOUND A1 - A5(A - DERIVATIVE)

\+ HCHO + R NH

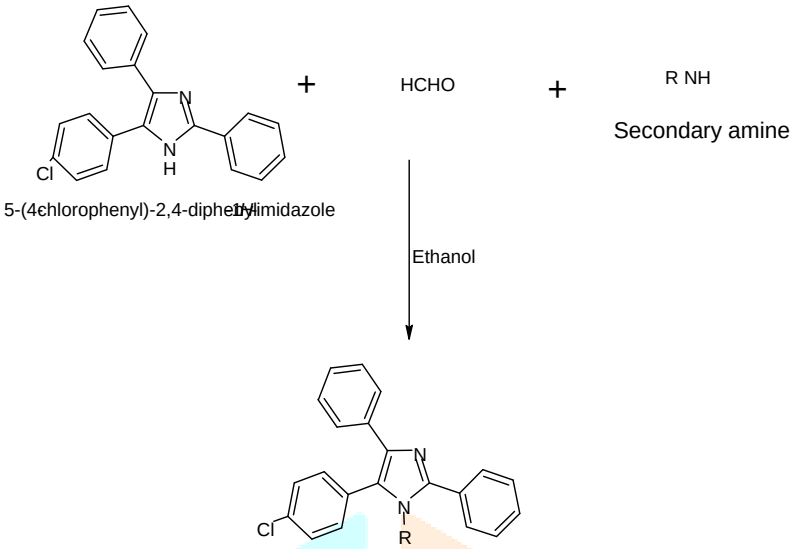
secondary amine

COMPOUND A -

COMPOUND	R
A1	Pyrrole
A2	Piperazine
A3	Diphenyl amine
A4	Pyrrolidine
A5	Dimethyl amine

STEP – II

PREPARATION OF SUBSTITUTED 5-(4-CHLOROPHENYL)-2,4-DIPHENYL-1H- IMIDAZOLE DERIVATIVES COMPOUND A6 – A10 (B - DERIV



5-(4-chlorophenyl)-2,4-diphenyl-1H-imidazole

- **Formaldehyde**

COMPOUND A6 - A10

COMPOUND	R
A6	Pyrrole
A7	Piperzine
A8	Diphenyl amine
A9	Pyrrolidine
A10	Dimethyl amine

- **EXPERIMENTAL PROCEDURE:-**

COMPOUND - A

STEP - I

PREPARATION OF 2,4,5 TRIPHENYL-1H- IMIDAZOLE

CHEMICAL REQURIEDS:

Benzil - 1gm

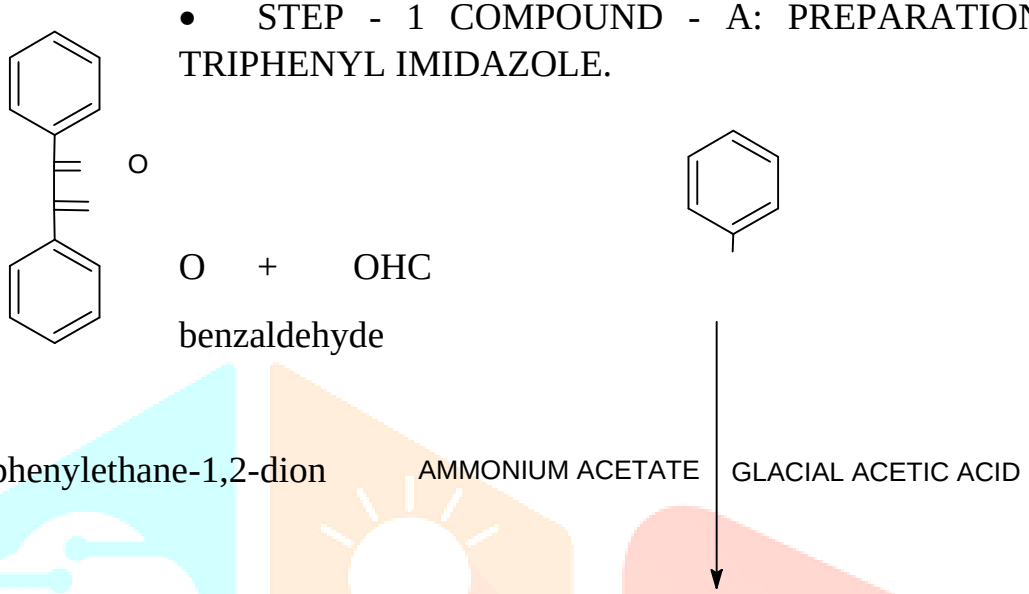
Ammonium acetate - 1gm

Glacial acetic acid - 2ml

- **PROCEDURE:-**

Benzyl (1gm),Ammonium acetate (1gm), Benzaldehyde(2ml),Glacial acetic acid(2ml) are reflux for 3hours.the reaction mixture was allowed to stand to attain room temperature. To that add 150 ml of water, the solid thus obtained was filtered. The filterate is neutralized with ammonium hydroxide or sodium carbonate to give solid pasty mass and filtered. Then the solid mass was washed with toluene and recrystalized from methanol.

- STEP - 1 COMPOUND - A: PREPARATION OF 2,4,5-TRIPHENYL IMIDAZOLE.



2,4,5-triphenyl-1*H*-imidazole

- **PHYSICAL DATA :-**

PHYSICAL DATA OF SYNTHESIZED COMPOUNDS

CODE	MOLECULAR FORMULA	MOLECULAR WEIGHT	I.U.P.A.C NAME
A1	C25H19N3	361.438	2,4,5 triphenyl-1-(1H-pyrrole-1-yl)-1H-imidazole
A2	C25H24 N4	380.484	2,4,5 triphenyl-1-(1H piperzine-1-yl) -1H-imidazole
A3	C33H25N3	463.57	N,N diphenyl-2,4,5triphenyl -1H-imidazol-1-amine
A4	C25H23N3	365.47	2,4,5 Triphenyl-1-(pyrrolidin-1-yl)-1H-imidazdazole
A5	C23H21N3	339.43	N,N dimethyl-2,4,5,triphenyl -1H-imidazol-1-amine
A6	C25H18ClN3	395.88	5-(4-Chlorophenyl)-2,4-diphenyl-1-(1H-pyrrole-1-yl)-1H-imidazole
A7	C25H23ClN4	414.92	5-(4-Chlorophenyl)-2,4-diphenyl-1H imidazole-1-yl piperzine
A8	C33H24ClN3	498.016	5-(4-chlorophenyl)N,N-diphenyl 2,4 diphenyl-1H-imidazol amine
A9	C25H22ClN3	399.91	5-(4-chlorophenyl) 2,4 diphenyl-1-(pyrrolidin-1-yl)-1H-imidazole
A10	C23H20ClN3	373.87	5-(4-chlorophenyl)-N,N-methyl-2,4diphenyl-1H-imidazol-1-amine

- **MELTING POINT :-**

COMPOUND	APPEARANCE	%YIELD	MELTING POINT -◦C	SOLUBILITY
A1	Brown solid	78	130	DMSO
A2	Sandal solid	72	110	DMSO
A3	White solid	75	125	DMSO
A4	White solid	77	140	DMSO
A5	Pale white solid	74	120	DMSO
A6	Dark brown solid	79	135	DMSO
A7	Pale orange solid	70	120	DMSO
A8	Pale yellow solid	68	100	DMSO
A9	White solid	71	130	DMSO
A10	Pale white solid	76	105	DMSO

- **THIN LAYER CHROMATOGRAPY:-**

The thin layer chromatography was used to determine the purity of the compounds in readymade silica gel plate and spots were visualized using iodine chamber.

SOLVENT SYSTEM USED:

HEXANE: ETHYL ACETATE

COMPOUND	C	H	N	Cl
	%FOUND			
	%CALCULATED			
A1	83.08	5.3	11.63	-
A2	78.92	6.36	14.73	-
A3	83.50	5.44	9.06	-
A4	82.16	6.34	11.5	-
A5	81.38	6.24	12.38	-

A6	75.85	4.58	10.6	8.96
A7	72.37	5.59	13	8.54

ELEMENTAL COMPOSITION ANALYSIS

- **SPECTRAL DATA :-**
- **MATERIALS AND METHODS:-**
- **INRFRED SPECTROSCOPY:-**

IR is concerned with study of absorption of infrared radiation, which results in vibrational transition.

Instrument – Shimazu FTIR

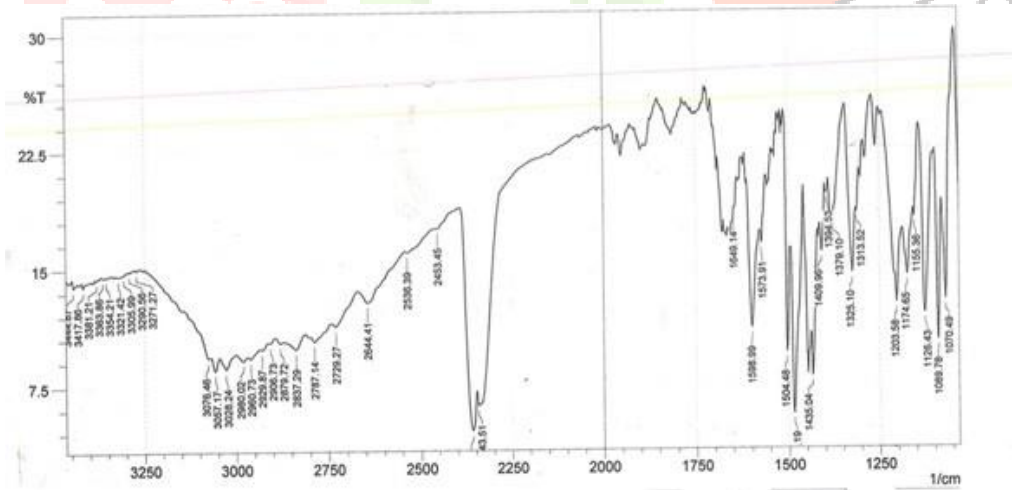
Region 4000 - 400cm^{-1}

Method - pressed pellet technique

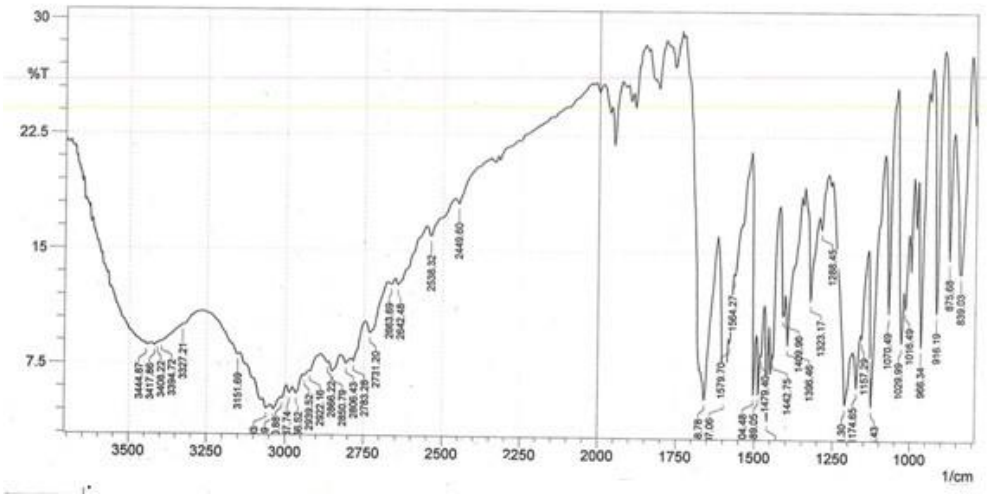
Values measured in cm^{-1}

- **INFRARED SPECTROSCOPY:-**

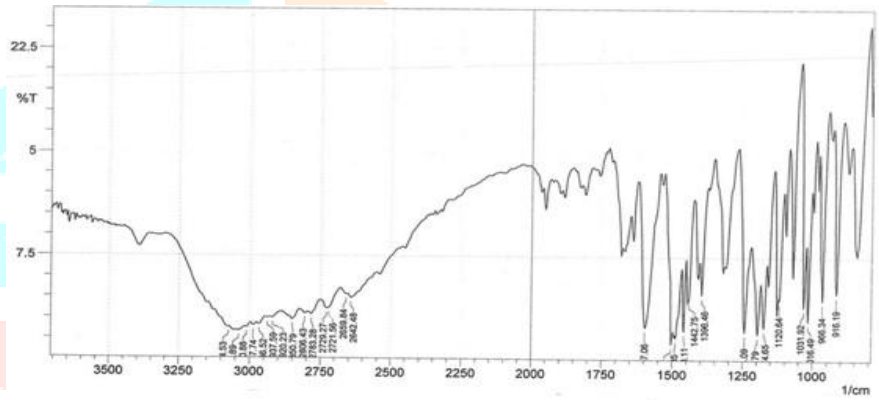
COMPOUND A1



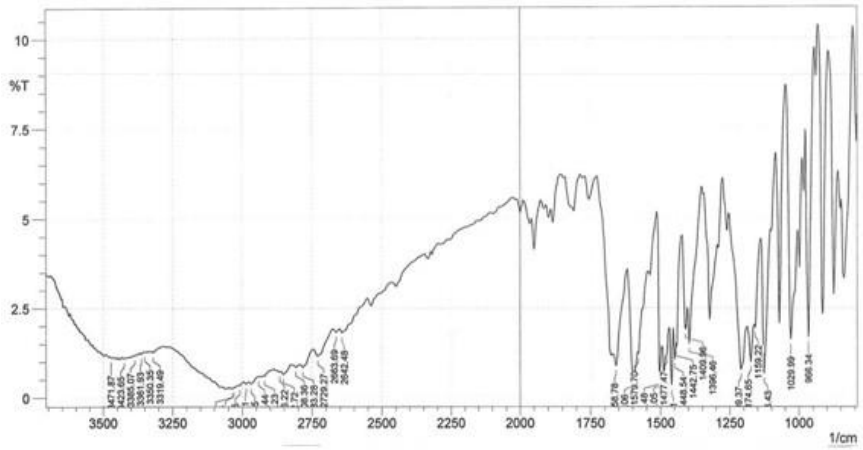
COMPOUND A2



COMPOUND A3



COMPOUND A4



CODE	TYPES OF VIBRATION	OBSERVED VALUE (cm^{-1})
A1	C=C str,in benzene CH str aromatic C – C str C – N str C = N str N – H str N – N str	1598 2960 1174 1325 1649 3028 3444
A2	C=C str,in benzene CH str aromatic C – C str C – N str C = N str N – H str N – N str	1597 2939 1174 1323 1658 3037 3444
A3	C=C str,in benzene CH str aromatic C – C str C – N str C = N str N – H str N – N str	1597 2920 1197 1244 1504 3010 3074
A4	C=C str,in benzene CH str aromatic C – C str C – N str C = N str N – H str N – N str	1597 2941 1174 1209 1658 3030 3471

- **BIOLOGICAL EVALUATION:-**
- Test concentration: 1. 100µg/ml.
  2. 200µg/ml.
- Organism used: 1. Bacillus subtilis.
  2. Klebsiella Pneumonia.
- Solvent Used: 1. DMSO
- Standard Drug: 1. Amikacin
- MEDIA PREPARATION: MULLER- HINTON AGAR MEDIUM:

- **INGREDIENTS:-**

Beef infusion - 300ml

Casein Hydrolysate - 17.5g

Starch - 1.5g

Agar - 10g

Distilled water

- **PROCEDURE:-**

Emulsify the starch in a small amount of cold water, pour into the beef infusion and add the casein hydrolysate and the agar. Make up the volume to 1litre with distilled water. Dissolve the constituents by heating gently at 100°C with agitation. Filter if necessary. Adjust the pH to 7.4. Dispense in screw-capped bottles and sterilized by autoclaving at 121°C for 20minutes and pour plates.

PREPARATION OF ANTIBACTERIAL SOLUTION:

All the test compound were dissolved in dimethyl sulfoxide and taken at two concentrations for testing antibacterial activity. The compounds were diffuse into the medium produced a concentration gradient. After the incubation period, the zone of inhibition was measured in mm.

- **EXPERIMENTAL PROCEDURE:**

The plates were inoculated by dipping a sterile swab into inoculums. The inoculation was dried at room temperature in aseptic condition. Ditch the bore in plate, to this bore add prepared antibacterial solution. These plates were placed in an incubator at 37°C within a few minutes

of preparation. After 48 hours of incubation the diameter of zone of inhibition was measured and reading observed in millimetre.

SAMPLE	BACILLUS	KLEBSIELLA	SAMPLE	BACILLUS
	100µg/ml	200µg/ml		100µg/ml
A1	R	9	A1	R
A2	6	17	A2	6
A3	10	15	A3	10

A4	8	14	A4	8
A5	11	16	A5	11
A6	R	9	A6	R
A7	15	21	A7	15
A8	R	12	A8	R
A9	R	14	A9	R
A10	7	16	A10	7
CONTROL	R	R	CONTROL	R

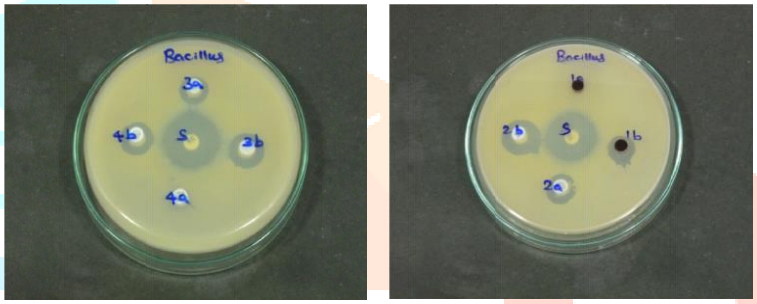


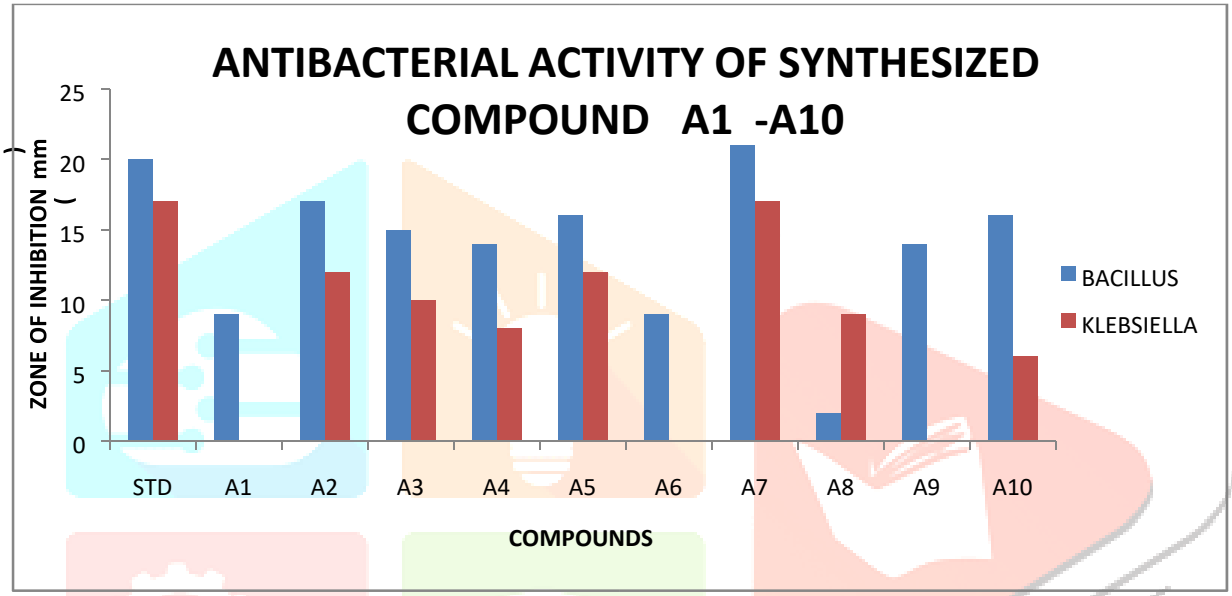
FIG-BACILLUS SUBTILIS

- **COMPOUND A1:- A10 AGAINST MICROBIAL AGENTS**

ORGANISM	BACTERIA		FUNGI	
COMPOUNDS	BACILLUS	KLEBSIELLA	CANDIDA	ASPERGILLUS
A1	9	-	7	-
A2	17	12	6	-
A3	15	10	10	-
A4	14	8	8	-
A5	16	12	11	-
A6	9	-	9	-
A7	21	17	7	9

A8	12	9	9	-
A9	14	-	12	6
A10	16	6	12	8
STD	20	17	21	18

- **ANTI MICROBIAL ACTIVITY**



- **Results :-**

The molecular design of synthesized compound were done by using different software.

The Lipinski rule was predicted for all synthesized compound using CHEMDOODLE.

The molecular formula, molecular weight and I.U.P.A.C name are predicted and shown in this work.

The percentage yield, melting point, solubility and appearance of the compound are determined.

The purity of the compounds was checked by TLC and Rf value was calculated. The results are here.

Elemental composition were found and calculated in percentage and results obtained are here.

The structure of the synthesized compounds was confirmed by IR spectra NMR spectra and Mass spectra.

IR spectra interpret value shown in this work.

NMR spectra interpret value shown in the project.

Mass spectra results are shown in this work.

All synthesized compounds were screened for their *invitro* antimicrobial activities.

The maximum zone of inhibition of synthesized compound against antimicrobial activity shown in this work.

All synthesized compound were tested for *invitro* anti-oxidant activity by reducing power assay method in different concentration and compared with the standard Ascorbic acid.

The result is shown in this work.

- **SUMMARY AND CONCLUSION :-**

Preliminary screening of novel 2,4,5 triphenyl derivative was done by using chemdoodle and molinspiration software.

The synthesized compounds were found to be identified by TLC.

All synthesized compounds were purified and characterized by the IR, NMR and

MASS spectrals datas.

The spectral datas were coinciding with the structure of synthesized compounds.

All the relevant peaks were identified in all the spectras.

The synthesized compounds were screened for *invitro* antimicrobial, anti-oxidant, antiarthritic activity and *in vivo* antiangiogenesis activity.

In vitro Antimicrobial activity:

The compound A7 shows potent antibacterial activity against bacillus subtilis and Klebsiella pneumonia compared to standard Amikacin.

The compound A9& A10 shows moderate antifungal activity against candida albicans compared to standard ketokonazole.The compound A7 minimum inhibition of antifungal activity against aspergillus niger compared to standard Ketokonazole.

Compound A7[5-(4-chlorophenyl)2,4, Diphenyl -1H imidazole 1-yl piperzine] having *in vitro* Anti-microbial, Antioxidant, Antiarthritic and *in vivo* Antiangiogenesis activity, As per my knowledge I conclude that compound A7[5-(4-chlorophenyl)2,4, Diphenyl -1H imidazole 1-yl piperzine] is the best compound compare than other than nine compounds.

- **REFERENCES:-**

1. *Nana V.Shitole, KiranF.Shelke, Swapnil S. Sonar, SandipA.Sadaphal, BapuraoB.Shingate and MurlidharS.Shingare,Bullkorean chem..soc.2009, Vol-30, No.9,P :1963-1966.*
2. *Vijayta Gupta and Vinay Kant, Science International. DOI co.5567/sci int.l.2013. 253-260.*
3. *Burungale Swati, MilindBhitre, Current Pharma Research ISSN;2230-7842. CPR 3(3),*
    a. *2013, 889-900.*
4. *Bhatnagar A., Sharma P.K.Kumar N.,IJPRIF ISSN: 0974-4304, Vol-3, No.1,P:268-282.JAN-MAR 2011*
5. *S.M.Ahmed, B.Pochaiah, M.C.Harikrishan, PharmaScient, Vol-1,Issue-1, 2012, 8-11. Bharti Ashish, Pandeya S.N, IJRAP 2011-2(4) , 1124-1129.*
6. *Gyanendra Kumar Sharma, Naveen Kumar Sharma and DevendarPathak, Indian Journal of Chemistry, Vol. 53B, Feb 2013, P:266-272.*
7. *Mohd Amir, IftikharAhsan, Wasin, Akhler, S.A.khan and Isar Ali, Indian Journal of*
    a. *Chemistry, Vol-50B,Feb 2011, P:207-213.*
8. *AdelA.Marzouk, VagifM.Abbasov, AvtandilH.Talybov, ShaabanKamelMohamed,World Journal of Organic Chemistry,2013, Vol-1, No-1, P:6-10.*
9. *Joseph sisko, Andrew J.Kassick, Mark Mellinger, John.John.J.Filan, Andrew Allen and*
    a. *Mark A.Olsen, J.Org.Chem 2000,65,1516-1524.*
10. *Jose Francisco civicos, Mohammed Gholinejad, Diego.A.Alonso and CormenNajera,*
    a. *Chem.Lett.2011,40, 907-909.*
11. *MazaahirKidwai, ShuchiKukreja, ShwetaRastogi and kavitaSinghal, Indian Journal of*
    a. *Chemistry,Vol-46B, Sep 2007,P:1549-1553.*