WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 8, Issue 1, 883-897. Research Article ISSN 2277– 7105

SYNTHESIS AND CHARACTERISATION OF 1,3,5 TRIPHENYL-2 PYRAZOLINE FOR ANTIMICROBIAL ACTIVITY

***Mr. Debraj De[1] and Assistant Prof. Mr. Sourav Saha[2]**

[1]B.Pharm, (B.Pharm –Bharat Technology, Uluberia, Howrah, West Bengal, India) and (M.Pharm-Calcutta Institute of Pharmaceutical Technology & Allied Health Sciences, West Bengal, Uluberia, Howrah, Pin-711316, India, Department of Pharmaceutics).

[2]M.Pharm, Department of Pharmaceutical Chemistry, Former Assistant Professor at Bharat Technology, Ulubria, Howrah, India. Currently: Assistant Professor at Global College of Pharmaceutical Technology, (Global knowledge Campus), Krishnanagar, Nadia, West Bengal. India.

Article Received on
25 October 2018,

Revised on 15 Nov. 2018,
Accepted on 05 Dec. 2018

DOI: 10.20959/wjpr20191-13859

***Corresponding Author**
Mr. Debraj De
B.Pharm, (B.Pharm –Bharat Technology, Uluberia, Howrah, West Bengal, India) and (M.Pharm-Calcutta Institute of Pharmaceutical Technology & Allied Health Sciences, West Bengal, Uluberia, Howrah, Pin-711316, India, Department of Pharmaceutics).

INTRODUCTION

Chalcone

Chalcones, considered to be the precursor of flavonoids and isoflavonoids, are abundant in edible plants. They consist of open-chain flavonoids in which the two aromatic rings are joined by a three-carbon α, β-unsaturated carbonyl system. Studies revealed that compounds with a chalcone-based structure have anti-inflammatory, anti-bacterial, anti-fungal, and anti-tumor activities. These activities are largely attributed due to the α, β- unsaturated ketone moiety. Introduction of various substituents into the two aryl rings is also a subject of interest because it leads to useful structure-activity relationship.[1][3][8]

Chemistry

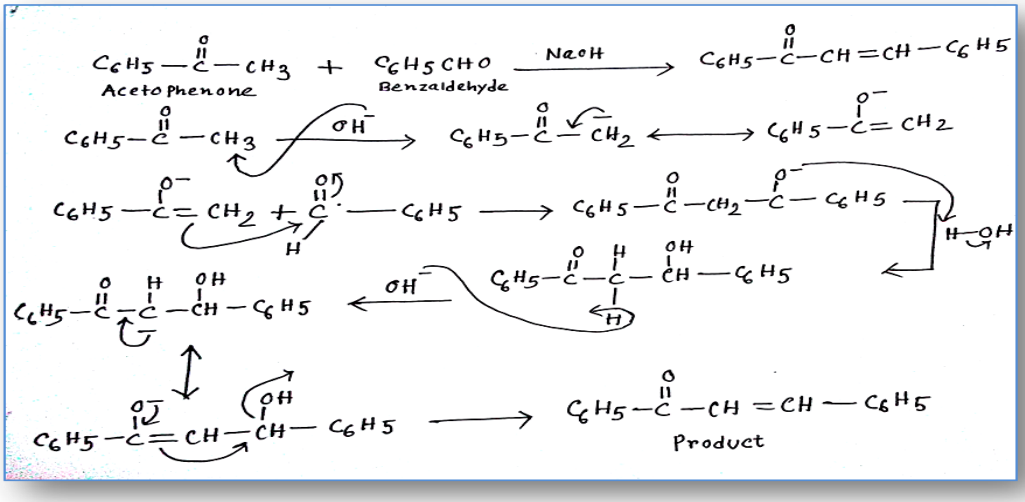
Chalcones are an important class of natural products and are considered as the precursors of flavonoids and isoflavonoids. Chemically, chalcones are 1,3- diaryl-2-propen-1-ones in which two aromatic rings are joined by a three carbon bridge having a carbonyl moiety and α,β unsaturation. Traditionally, chalcones are prepared by Claisen-Schmidt condensation of equimolar concentrations of arylaldehydes and acetophenones which are generally base

catalysed. One of the important class of reactions of chalcones are the ring closure reactions with hydrazine, phenylhydrazine, guanidine, urea etc producing heterocyclic derivatives of chalcones. Both chalcones and their heterocyclic derivatives have a number of pharmacological activities such as antiinflammatory, antimicrobial, antifungal, antibacterial, antioxidant, cytotoxic, antitumor, anticancer, antimitotic, antileishmanial, anti-malarial, antitubercular, antiviral, and so on. In this efforts have been made to throw some light on the synthesis and biological activities of chalcones and their derivatives.

Chalcones are a major class of natural products belonging to the flavonoid family. They are considered as the precursors of flavonoids and isoflavonoids. They are also the precursors of a number of biologically important heterocycles such as benzothiazepines, pyrazolines, and flavones. They are widely distributed in fruits, vegetables, tea, spices, soy based foods and other plant products. Chemically, chalcones are 1,3-diaryl-2-propen-1-ones in which two aromatic rings or substituted aromatic rings are joined together by a three carbon atom α, β unsaturated carbonyl system. They have the following general structure.

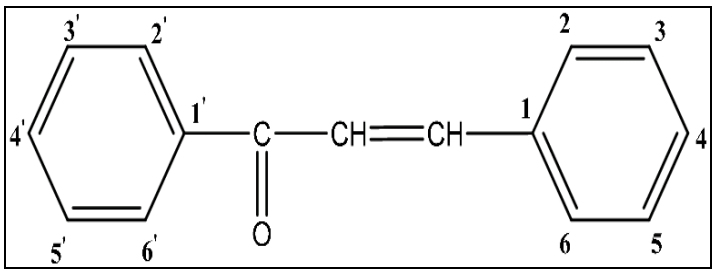
Claisen-Schimdt Condensation

Different methods are available for the preparation of chalcones. The most convenient method is the Claisen-Schimdt condensation of equimolar quantities of arylmethylketone with aryl aldehyde in the presence of alcoholic alkali. In the Claisen Schmidt reaction, the concentration of alkali used usually ranges between 10 to 60%. The reaction is carried out at room temperature for 24 hours. Under these conditionsthe Cannizarro reaction also take place and thereby decreases the yield of the desired product. To avoid the disproportionation of aldehyde in the above reaction theuse of benzylidene diacetate in place of aldehyde was recommended. The concept of "Microwave Induced Organic Reaction Enhancement" chemistry has proved very useful in the efficient synthesis of chalcones and relatedenone. The procedure involves condensation of ketones and aromatic aldehydes with ethanol as energy transfer medium. This process is carried out in the presence of sodium hydroxide in open glass vessel under microwave irradiation. The obtained products have better yield and rate of reaction has also been enhanced. The reaction time is reduced from hours to minutes, thus providing the versatility of the process. The mechanism is as follows.



Benzalacetophenone

Structure and Properties



IUPAC name 1, 3-Di(phenyl)prop-2-en-1-one

Chemical formula C15H12O

Properties

Chemical class Carbonyl compounds

Boiling point 345°C - 348°C

Melting point 57°C -58°C

Appearance yellowish white crystalline

Solubility soluble in hot ethyl alcohol

Biological Activities

Benzalacetophenone is an important class of compounds because they possess important biological activities like:

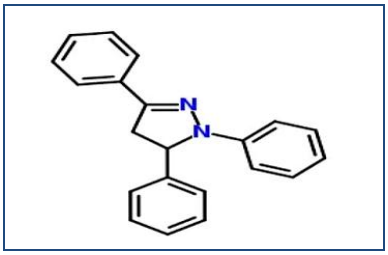
1) Antimicrobial activity and Antifungal activity.

2) Antimalerial activity.

3) Artificial sweetaners etc.

1,3,5-Triphenyl -2-Pyrazoline

Structure and Properties



IUPAC name 1,3,5-TRIPHENYL -2-PYRAZOLINE

Chemical formula C21H18N2

Properties

Chemical class Pyrazoline

Melting point 86°C -87°C

Appearance Yellowish powder

Solubility Soluble in hot ethyl alcohol

Biological Activities

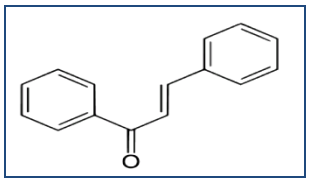
1,3,5-Triphenyl-2-pyrazoline is an important class of compounds because they possess important biological activities like:

1) Antimicrobial activity.
2) Antifungal activity.
3) Cytotoxic activity.
4) Antimalerial & Anticarcinogenic activity.
5) Artificial sweetaners etc.

Review of Literature

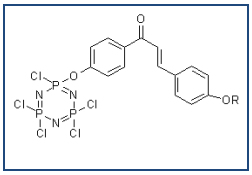
1) B. B. Chavan *et al.*, were synthesized "Synthesis and Medicinal Significance of Chalcones- A Review"

The presence of a reactive alpha, beta-unsatutated keto function in chalcones is found to be responsible for their antimicrobialactivity. In this paper through reviewing different biological significance of chalcones andtheir derivatives have been reported along with their chemistry and of synthesis.[1]



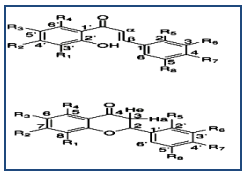
2) N. BT. Mahsir *et al.*, were synthesized **"**Synthesis and Characterization of Cyclophosphazene Bearing Chalcones Derivatives**"**

This research involves the synthesis of chalcones derivative with hexachlorocyclotriphosphazene, a type of cyclophosphazene to produce a compound withflame retardant properties.[2]



3) A. S. Albogami *et al.*, were synthesized "Simple and Efficient One Step Synthesis of Functionalized Flavanones and Chalcones"

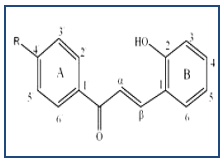
A facile and highly efficient microwave-assisted synthesis of functionalized chalcones andflavanones based on the Claisen-Schmidt condensation reaction is reported. The method describes the synthesis of flavanones in single step with excellent yield and it was revealed that position and number of substituents on acetophenones and aromatic aldehydes played a very crucial and key role in the construction of flavanone derivatives. Among the thirty two synthesized compounds, five chalcones and one flavanone were novel compounds.[3]



4) S. Syam *et al.*, were synthesized "Synthesis of Chalcones with Anticancer Activities"

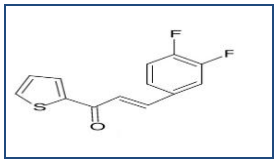
Several chalcones were synthesized and their *in vitro* cytotoxicity againstvarious human cell lines, including human breast adenocarcinoma cell line MCF-7, humanlung adenocarcinoma cell line A549, human prostate cancer cell line PC3, humanadenocarcinoma cell line HT-29 (colorectal cancer) and human normal liver cell lineWRL-68 was evaluated. Most of the compounds being active cytotoxic agents. The ROS level showed 1.3-fold increase ($p < 0.05$) at the low concentrations used and thus itwas concluded that the compounds increased the

ROS level eventually leading to apoptosisin MCF-7 cells through intrinsic as well as extrinsic pathways.[4]



5) M. Y. Mowlana *et al.,* were synthesized "Synthesis, Characterization and Microbial Activities of Novel Acetylthiophene Chalcone Derivatives"

Synthesis of Chalcones from acetylthiophene with substituted aromatic aldehyde in dilute ethonolic sodium hydroxide at coolcondition reaction followed by Claisen – Schmidt condensation method. The antibacterial and antifungal activity was evaluated against Klebsiella aerogenes, Proteus Vulgaris, Mucor racemosus, Aspergillus flavous and Aspergillus fumigatous(fungal strain) using Ciprofloxacin and Nystatin as thestandard drug for bacteria and fungus respectively.[5]



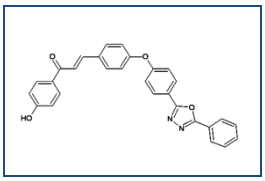
6) S. A. Hasan *et al.,* were synthesized "Synthesis, characterization and antimicrobial evaluation of a series of chalcone derivatives"

To synthesis a series of six chalcones that resemble those occur in nature and to evaluate the in vitro antimicrobialactivity of these chalcones against Gram positive and Gram negative bacteria and fungi. Chalcones weresynthesized from acetophenone and substituted benzaldehydes via the Claisen-Schmidt condensation.[6]

7**) C. K. Thasneem *et al.,*** were synthesized "Synthesis And Antimicrobial Study Of Chalcone Linked 1,3,4-Oxadiazole Derivatives"

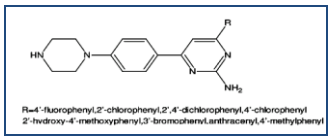
Synthesis of chalcone linked 1, 3, 4 – oxadiazole were carried out by clubbing of substituted chalcone and substituted oxadiazole. Purity of the compounds ascertained consistency by

TLC and melting point determination. The structure of newly synthesized compounds were characterized by IR, HNMR, MAS Spectral analysis and evaluated for antimicrobial activity on bacteria (both gram +ve and -ve) and fungai. The derivatives showed significant activity on both bacteria and fungai.[7]



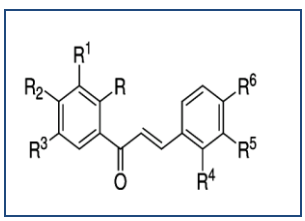
8) R. Ghosh *et al.,* were synthesized "Synthesis And Biological Activities Of Chalcones Andtheir Heterocyclic Derivatives: A Review"

One of the important class of reactions of chalcones are the ringclosure reactions with hydrazine, phenylhydrazine, guanidine, urea etc. producing heterocyclic derivatives of chalcones. Both chalcones andtheir heterocyclic derivatives have a number of pharmacological activities such as antiinflammatory, antimicrobial, antifungal, antibacterial, antioxidant, cytotoxic, antitumor, anticancer, antimitotic, antileishmanial, anti-malarial, antitubercular, antiviral, and so on. Inthis review efforts have been made to throw some light on the synthesis and biologicalactivities of chalcones and their derivatives.[8]



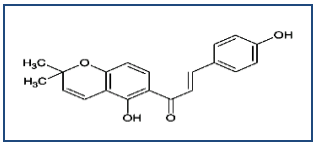
9) J. K. Makrandi *et al.,* were synthesized "An efficient green procedure for the synthesis of chalcones using C-200 as solid support under grinding conditions"

A simple, rapid, efficient and environmentally benign procedure for the synthesis of chalcones has been achieved by grinding aryl aldehydes and acetophenones with anhydrous barium hydroxide (C-200) in the absence of any solvent. The use of organic solvent for extraction of compound is also avoided. This present method is highly useful for the synthesis of 2?-hydroxy chalcones, required intermediates for the synthesis of flavanoids.[9]



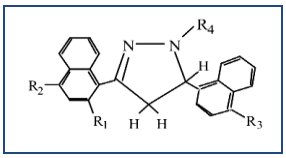
10) D. I *et al.,* were synthesized "Synthesis and Antimalarial Activities of Chalcone Derivatives".

Quinoxaline Chalcones, Quinolinyl Chalcones, Chalcone Sulphonamides, Licochalcones And Morachalcones Have Been Reported To Possess Good Antimalarial Property. Some Chalcones Have Also Been Reported To Show Fascinating Antimalarial Activities Against Chloroquine Resistant *P. Falciparum* Strain. The Methods Of Chalcone Synthesis Have Been Improved From The Usual Conventional Methods To Microwave Assisted Protocols Leading To Drastic Reduction In Time Required For The Synthesis And As Well Improved Yield.[10]



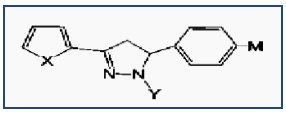
11) D. Azarifar *et al.,* were synthesized "Synthesis and Characterization of New 3,5-DinaphthylSubstituted 2-Pyrazolines and Study of Their Antimicrobial Activity"

A number of chalcones were prepared by condensing either 1-acetylnaphthalene or substituted 1-acetylnaphthalenes with 1-naphthaldehyde or 4-dimethylamino-1-naphthaldehyde in ethanolic NaOH solutions. These chalcones were immediately reacted with hydrazine hydrochloride, phenyl hydrazine and semicarbazide hydrochloride in the presence of dry acetic acid to obtain the corresponding2-pyrazolines.[11]



12) N. L. Shihabaldain *et al.,* were synthesized "Synthesis and characterization of some new pyrazolines derivatives and their biological activity"

Six different hydrazine's (hydrazine hydrate 80%, phenyl hydrazine, thiosemicarbazide, semicarbazide, 2,4- dinitrophenyl hydrazine and 4- phenyl thiosemicarbazide) were reacted with six different types of substituted chalcones α,β- unsaturated ketenes to yield pyrazole derivatives then characterized the products with infrared spectra, elemental analysis, mass spectra, 1H and 13C-NMR spectra. Finally their biological activity for some of the new pyrazoles were studied.[12]



AIMS AND OBJECTIVES

1) To synthesize 1,3,5 triphenyl-2-pyrazoline from Benzalacetophenone.

2) Characterisation of the synthesized compound by physical parameters, uv-spectroscopy and FTIR spectroscopy.

- Aim of the present work is to synthesize 1,3,5 triphenyl-2-pyrazoline. As the literature review reveals that benzalacetophenone is a bioactive lead molecule for synthesizing newer drug and have potent antimicrobial activity and is also used for sweetening agent and have cytotoxic activity is commercially important for industrial practice.

MATERIALS AND METHODS

Materials

CHEMICALS	SOURCE
Acetophenone	Merck laboratory, India
Benzaldehyde	Merck laboratory, India
Sodium hydroxide	Loba chemical, India
Rectified spirit	Loba chemical, India
Phenyl Hydrazine	Merck laboratory, India
Ethanol	Jiangsu Huaxiinternational trade co.
Acetic acid	Merck laboratory, India
Distilled water	Laboratory

APPARATUS	SOURCE
Round bottom flask	Borosil
Beaker	Borosil
Measuring cylinder	Borosil
Glass rod	Borosil
Reflux condenser	Borosil
Capillary tube	Borosil
TLC plate	Silica
Buchner funnel	Phorsheline

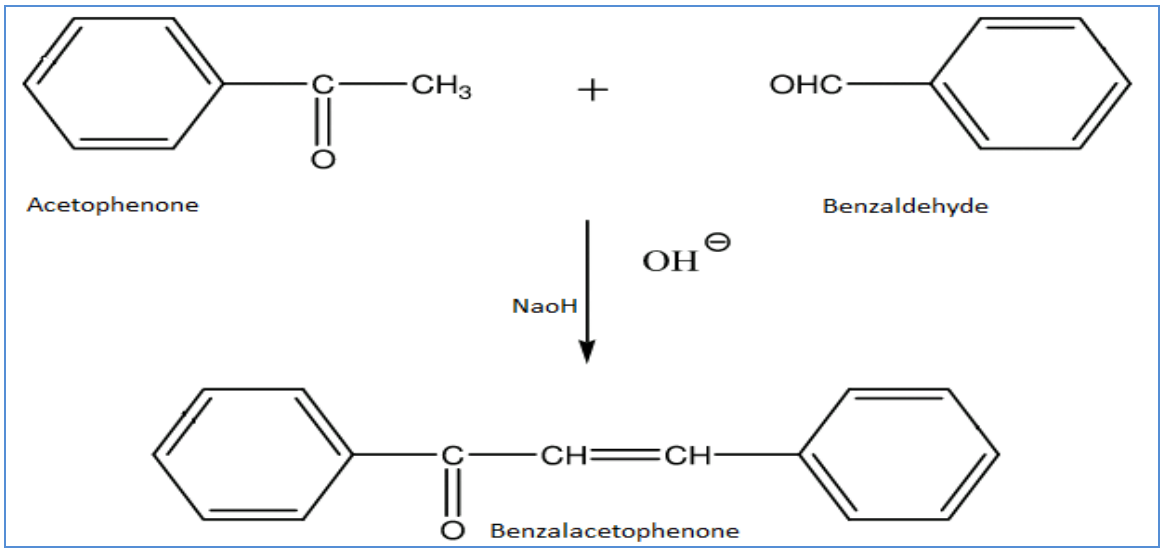
INSTRUMENTS	MODEL
Hot air oven	Testing instrument mfg.co
Water bath	Testing instrument mfg.co
Digital balance	Accurate weighing.sys AZT 300
Suction pump	Tottlits Eng.co.ISP25
Heating mental	Oshan
FTIR	Shimadzu
UV-visible spectrophotometer	Shimadzu1700 double beam

METHOD

Schematic representation

Step-1

- **Scheme of Benzalacetophenone synthesis**



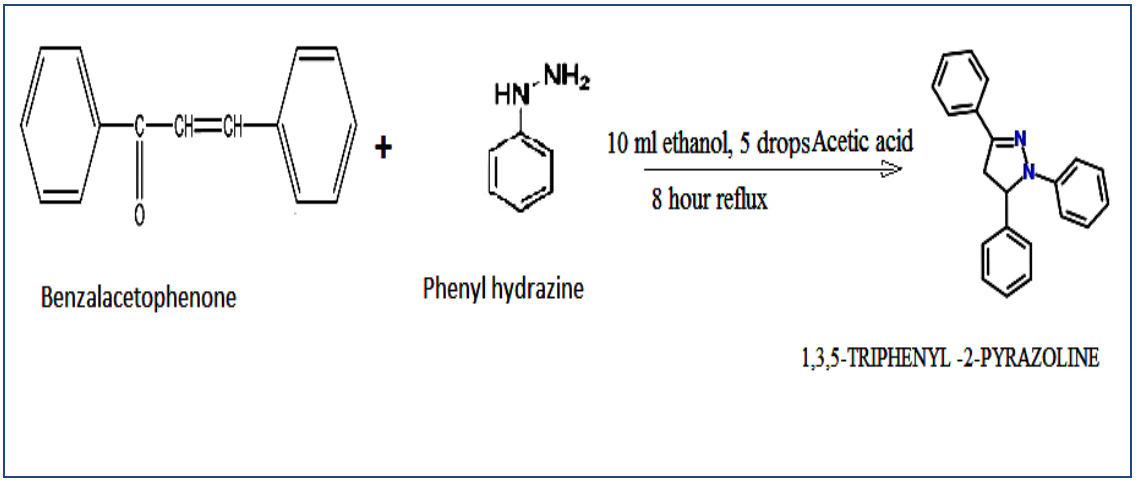
- **Preparation of Benzalacetophenone**

Place a solution of 5 gm of NaOH in 40ml of water and 30ml of rectified spirit in an iodine flask. stirr in magnetic stirrer. Immerse the flask in ice bath and 12ml of Acetophenone and start stirrering then add 11ml of pure Benzaldehyde, keep the temperature about 25°C and stirrer vigorously for 2 hours. Remove the flask from the stirrer and stand the reaction mixture in refrizerator over night. Filter the product and wash with water. Then the product is dried.

Compound	**DDAC/B01 A**
IUPAC name	1, 3-Dipheny lprop-2-en-1-one
Molecular formula	C15H12O
Molecular weight	208
Melting point	57°C -58°C
Percentage yield	89.7%

Step-2

- **Scheme of 1,3,5-Triphenyl -2-Pyrazoline synthesis**



- **Preparation of 1,3,5-Triphenyl -2-Pyrazoline**

Equimolar amount of Benzalacetophenone and equimolar amount of Phenylhydrazine are taken and transferred to round bottom flask.10ml ethanol is added to the mixture. 4-5 drops of acetic acid is added in the mixture. Then it is refluxed for 8 hours.

Compound	**DDAC/B01 B**
IUPAC name	1,3,5-TRIPHENYL -2-PYRAZOLINE
Molecular formula	C21H18N2
Molecular weight	285
Melting point	86°C -87°C
Percentage yield	78.3%

RESULT AND DISCUSSION

The synthesized compounds were characterized on the basis of

- Physical parameter
- Determination of λ_{max} by UV-visible spectrophotometer
- Identification of functional group by FTIR analysis.

Physical Parameter

Physical parameters like physical state (colour, nature), solubility, percentage of yield, molecular weight, melting point were determined.

Determination of λ_{MAX} by uv-Visible Spectrophotometer

The λ_{max} of the synthesized compound was scanned in pure ethanol and using ethanol as blank in different concentration in a double beam UV-visible spectrophotometer.

Identification of Functional Group by Ftir Analysis

Presence of different functional group is synthesized compound were identified by interpreting FTIR graph. The graph was taken by prepairing solid sample for IR by KBr pellet method. The thoroughly dried KBr is grounded with sample (100:1::KBr:sample) ratio. The pellets were prepared in a hydrolic KBr press.

Physical Parameters Check

Compound	DDAC/B01 A	DDAC/B01 B
IUPAC name	1, 3-Di(phenyl)prop-2-en-1-one	1,3,5-Triphenyl -2-Pyrazoline
Molecular formula	C15H12O	C21H18N2
Molecular weight	208	285
Nature	Yellowish white crystalline	Solid yellow crystalline
Colour	Yellowish white	Light yellow
Solubility	Ethanol	Hot Ethanol
Percentage of yield	89.7%	78.3%
Melting point	57°C -58°C	86°C -87°C

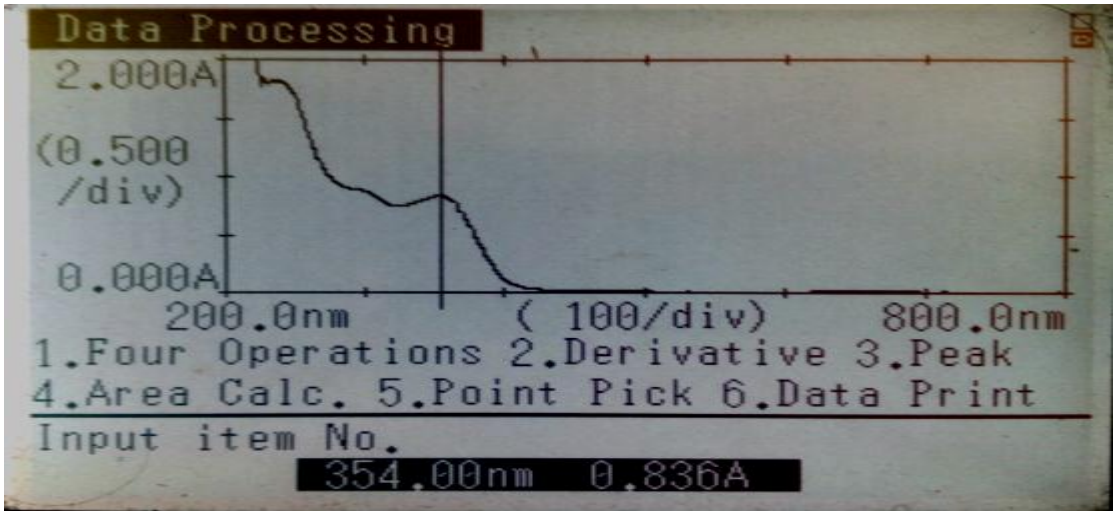
- **λ_{MAX} Determination**

λ_{max} had been determined in Shimadzu 1700 double beam spectrophotometer using Ethanol as a solvent for the synthesized compound DDAC/B01 B.

- **Sample Preparation(Liquid)**

A specific amount of compound DDAC/B01 A was dissolved in glacial acetic acid and the mixture was diluted to a specific extent. This sample solution was placed in cuvette and analysed in spectrophotometer against glacial acetic acid(blank solution).

UV-VIS Spectroscopy



Wavelength(nm)	Absorbance
354.00	0.836

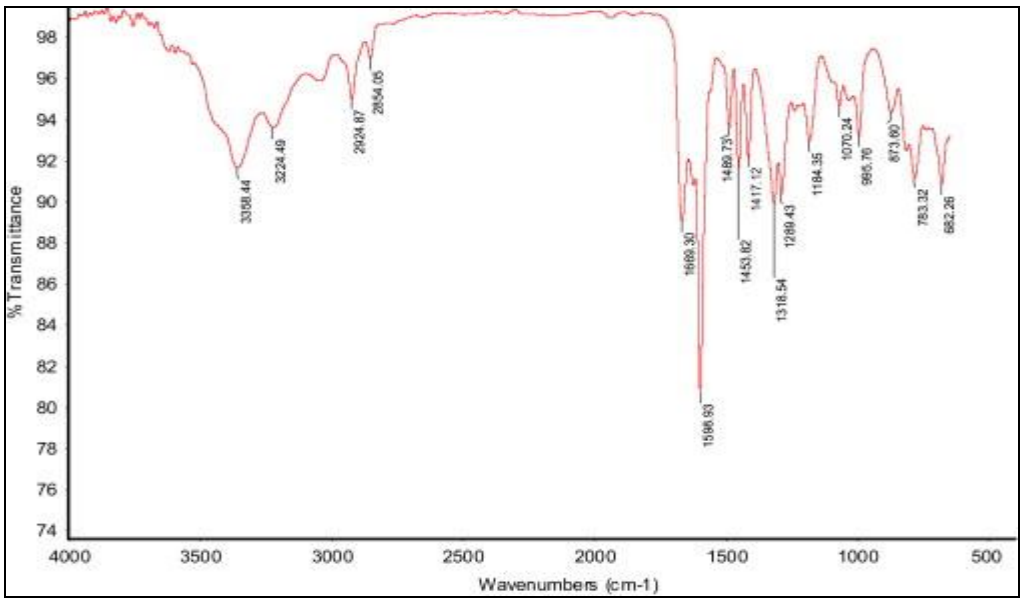
- **Infra Red Spectrum Analysis**

IR spectroscopic analysis had been carried out in FTIR -8400, Fourier transform (SHIMADZU) Infra red spectrophotometer using potassium bromide for the synthesized compound.

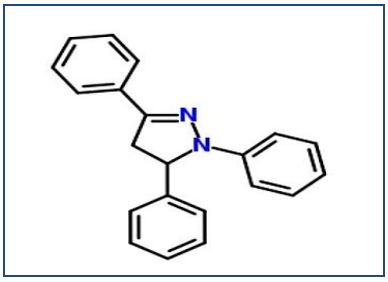
- **Sample Preparation(Solid)**

Solid for the infra red spectrum may be examined as an alkali halide mixture. Alkali halide usually sodium chloride which was transparent throughout the infra region was commonly used for the purpose. The solid substance is ground with KBr and made into a disc with the help of KBr press model M-15(technology instruments) after drying and press at high pressure. Also a blank disc is prepared with KBr which may be placed in the path of the reference beam.

Infra Red Spectroscopy Graph



Infra Red Spectrum of compound DDAC/B01 B



N-H Stretching	**3453.27**
N-H Bending	**1547.44**
C=N Stretching	**1642.75**
N-C Vibration	**1395.33**
C=C Stretching(Aromatic)	**1516.48**

➢ CONCLUSION

From the above content it can be clearly concluded that major chalcone derivative "1,3,5-Triphenyl -2-Pyrazoline" was synthesized and characterized.

The substitute Pyrazoline moieties are already known for different biological activities. 1,3,5-Triphenyl -2-Pyrazoline is significantly known for antibacterial activity.

From the above result one can establish that the synthesized substituted Pyrazoline can be rich source for exploitation. Therefore in search of new generation of the active compounds, it may be worthwhile to explore possibility in this area by making or introducing different functional groups. Which may result into better anti-bacterial activity.

➢ Future Work Plan

Derivatives of chalcone are of great importance in the antibacterial activity. I followed the general synthesis of 1,3,5-Triphenyl -2-Pyrazoline derivatives and I perform its Spectroscopical analysis and FTIR.

My future work plan on this topic is to progress further with general synthesis procedure to synthesize more derivatives of Chalcone, their charecterization and most importantly to found some more potent anti-bacterial compound.

➢ REFERENCES

1. B. B. Chavan *et al.*; "Synthesis and Medicinal Significance of Chalcones- A Review", Asian Journal of Biomedical and Pharmaceutical Sciences, 2015; ISSN: 0135-450; 19: 1-6.
2. N. Bt. Mahsir *et al.*; "Synthesis And Characterization Of Cyclophosphazene Bearing Chalcones Derivatives"; International journal of Medical sciences, 2008; ISSN: 1003-0097; 43: 1-16.
3. A. S. Albogami *et al.* "Simple and Efficient One Step Synthesis of Functionalized Flavanones and Chalcones"; Oriental Journal Of Chemistry, 2007; ISSN: 0970-020, 28: 619-626.

4. S. Syam *et al.*; "Synthesis of Chalcones with Anticancer Activities" European journal of Chemistry, 2003; ISSN: 1420-3049; 65: 6180-6195.
5. M. Y. Mowlana *et al.*; "Synthesis, Characterization and Microbial Activities of Novel Acetylthiophene Chalcone Derivatives" International Journal of Science and Research (IJSR), 2014; ISSN: 2319-7064; 3: 54-56.
6. S. A. Hasan *et al.;* "Synthesis, characterization and antimicrobial evaluation of a series of chalcone derivatives" Indian journal of Chemistry 2013; ISSN 0975-413, 7: 39-42.
7. C. K. Thasneem *et al.;* "Synthesis And Antimicrobial Study Of Chalcone Linked 1,3,4-Oxadiazole Derivatives". World Journal Of Pharmacy And Pharmaceutical Sciences, 2011; ISSN: 2278 – 4357, 4: 643-655.
8. R. Ghosh *et al.*; "Synthesis And Biological Activities Of Chalcones Andtheir Heterocyclic Derivatives: A Review" World Journal Of Pharmacy And Pharmaceutical Sciences, 2008; ISSN 2278 – 4357; 3(3): 578-595.
9. S. Kumar *et al.*; "An efficient green procedure for the synthesis of chalcones using C-200 as solid support under grinding conditions" International journal of Biomedical sciences, 2003; ISSN: 1751-8253; 1: 123-125.
10. I. Ugwu *et al.;* "Synthesis and Antimalarial Activities of Chalcone Derivatives" International Journal of Chem Tech Research, 2010; ISSN: 0974-4290; 7: 1966-1984.
11. D. Azarifar *et al.*; "Synthesis and Characterization of New 3,5-Dinaphthyl Substituted 2-Pyrazolines and Study of Their Antimicrobial Activity" European journal of Medicines, 2005; ISSN 1420-3049; 2(5): 885-895.
12. K. S. Saud *et al.*; "Synthesis and characterization of some new pyrazolines derivatives and their biological activity" Journal of Chemical and Pharmaceutical Research, 2015; ISSN: 0975-7384; 7(12): 1042-1055.
13. Dr. S. R. Sankar, Text Book Of Pharmaceutical Analysis, Rx publications, Fourth edition, 2010; 2-1 – 5-7.
14. G. R. Chatwal, Instrumental Methods Of Chemical Analysis, Himalaya Publishing House, Edition, 2010; 2.29-2.184.
15. B. S. Furniss, Vogel's Textbook Of Practical Organic Chemistry, Pearson Education, Fifth Edition, 2005; 1034-35.