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Synthesis, Characterization and Biological Activity of Newly Synthesized Benzoic Acid and Phenylthiourea Derivative

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Abstract: *Benzoic acid, a simple aromatic carboxylic acid, has a rich history of use and study due to its diverse biological activities and applications. Historically, it has been known since ancient times, originally obtained from natural sources like gum benzoin, and later synthesized for industrial use. The synthesis of benzoic acid has evolved from early methods such as the oxidation of toluene to more modern, efficient techniques involving catalytic reactions. The structure of benzoic acid consists of a benzene ring with a carboxyl group (-COOH) attached, which contributes to its acidic properties and influences its reactivity. The structure-activity relationship (SAR) of benzoic acid is characterized by its ability to interact with a variety of biological targets, with modifications to the aromatic ring or the carboxyl group affecting its potency and specificity. Benzoic acid derivatives, such as esters and salts, exhibit a wide range of applications in medicine, agriculture, and the food industry. It is used as an antimicrobial agent, a food preservative, and a precursor in the synthesis of various pharmaceutical. The mechanism of action of benzoic acid and its derivatives typically involves the disruption of cellular processes through their acidic nature, interactions with enzymes, or membrane disruption. In the pharmaceutical field, benzoic acid's derivatives exhibit anti-inflammatory, antimicrobial, and anticancer properties. The compound's widespread applications and continued research into its bioactivity make it an essential molecule in various scientific and industrial domains..*

Keywords: Benzoic acid, History, Preservatives, Antimicrobial activity , Synthesis, Structure activity Relationship, mechanism of action

I. INTRODUCTION

Benzoic acid is a compound consisting of a benzene ring attached to a carboxylic acid group is a white, crystalline solid with a characteristic odour, commonly used as a food preservative, Antifungal agent and Pharmaceutical Intermediate, benzoic acid and Its derivatives have been Extensively studied for their diverse biological activities Including antimicrobial, anti-Inflammatory antioxidant & anticancer properties Historically, benzoic acid was first Isolated from gum benzoin, a resin obtained from the Bark of certain trees in the genus styrax Today, benzoic acid Is produced Industrially through Benzamide and oxidation of toluene or other aromatic hydrocarbons. posed by antibiotic resistance. Benzoic acid is a white or colorless solid that is made up of a benzene ring attached to a carboxyl group (−COOH). It has the chemical formula C6H5COOH and weighs 122.1 g/mol. The substance appears as a white crystalline powder and is only slightly soluble in water (about 2.9 g/l at 20°C) but dissolves easily in ethanol. It is the simplest type of aromatic carboxylic acid. Benzoic acid got its name from "gum benzoin," which was once the primary source of this compound. It can be found naturally in many plants and is involved in the production of various secondary metabolites in plants. Additionally, benzoic acid has a unique effect on
human biology, where it helps inhibit a process called macroautophagy, which has led to its use as a food preservative. Benzoic acid is a common organic compound found in everyday products like food, cosmetics, and personal care items.

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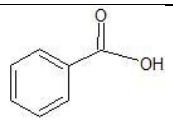
It's often used as a preservative in products such as pickles, jams, lipsticks, and face creams. Additionally, benzoic acid plays an important role as a building block in the creation of many other organic compounds.

Benzoic acid is part of a larger group of chemicals called phenolic substances, which include flavonoids and other carboxylic acids. These compounds help plants protect themselves from microbes and also play a role in plant interactions with microbes. Some phenolic compounds have antimicrobial properties and are involved in plant defense. They are categorized into two groups: phytoalexins (produced in response to stress or infection) and phytoanticipins (pre-existing in the plant). While it is well-known that these compounds help protect plants from fungal infections, it is not always clear whether a specific phenolic compound or its breakdown product is responsible for the effect

It is solid substance commonly used in cosmetics to help maintain the product's pH and act as a preservative. It has the European approval number E210. Preservatives like benzoic acid are added to products to prevent spoilage, extend shelf life, and stop harmful bacteria or fungi from growing. These preservatives are carefully regulated to ensure they don't negatively affect the product's quality or safety. Additives and preservatives are given an E-number, which means they have been tested for safety. Some common preservatives include sorbic acid, propionic acid, and benzoic acid, with parabens being widely used in cosmetics. However, these chemicals can sometimes cause allergic reactions, migraines, asthma attacks, and may even be linked to issues like obesity or behavioral problems, especially in children.

DRUG PROFILE:

Name	Benzoic acid
IUPAC name	Benzene carboxylic acid
Molecular formula	$C_7H_6O_2$
Molecular weight	122 g/mol
Structure	 Benzoic Acid
Theoretical yield	5 g
Practical yield	4.5 g
Appearance	Colourless crystalline solid
Solubility	In water and ethanol
Category	Antimicrobial, Anti inflammatory

MATERIALS AND METHOD

Material required:

Benzoic acid as a precursor for functionalization.

• Phenylthiourea (or derivatives) as a thiourea source.

• Synthesis Methodology:

• Coupling Reaction: A condensation reaction between benzoic acid and phenylthiourea or Derivatives could yield benzoic acid-phenylthiourea hybrids.

• Reagents & Solvents: Common reagents such as catalysts (e.g., acid/base), and solvents (e.g., ethanol, DMF) might be used. • Temperature and Time: Optimization of reaction conditions (e.g., temperature, reaction Time) to maximize yield and purity.

Method: The acid-catalysed hydrolysis of benzamide is a reliable method for producing benzoic acid. It involves the reaction of benzamide with water in the presence of an acid catalyst, resulting in the formation of benzoic acid and ammonium ion.

Synthesis of Benzoic acid

Apparatus: Iodine flask, beaker, measuring cylinder, glass rod, water bath, funnel, tripod Stand

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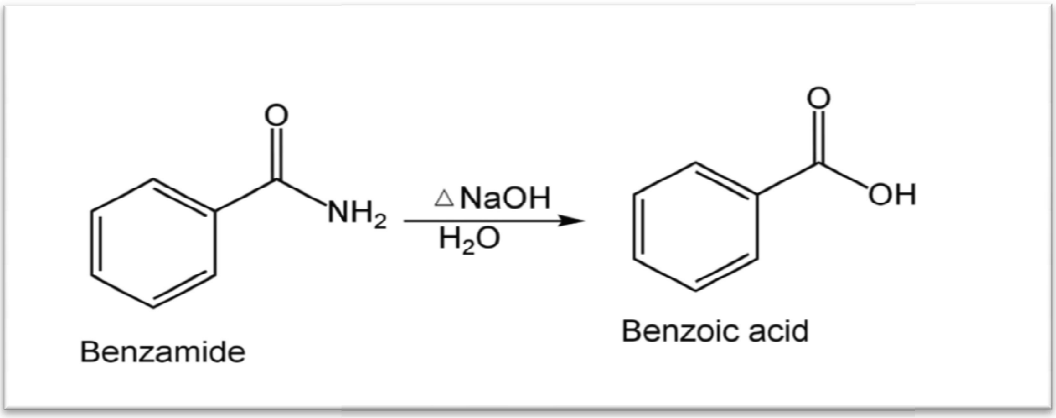
Chemicals: Benzamide ,10% sodium hydroxide, conc. Hydrochloric acid, Ice water



Reaction:

Procedure:

1. 5 g of benzamide was taken in a 250 mi Iodine flask.
2. 75 ml of 10% NaOH was added in flask & frequently shaken.
3. When mixture get dissolved porcelain piece was added in flask to avoid bumping of Mixture. The reaction mixture was kept closed with Stopper .
4. Reaction mixture was kept in water bath for 30 min to occur the reaction
5. After that, reaction was completed. The flask was kept in cold Ice Water bath for 5-6 Minutes When mixture was cooled conc. HCl added drop wise until all product separate Out reaction mixture was again cooled in ice water bath about 10 min.
6. Compound was filtered through the funnel was formed in crystalline state But as it Contain some impurities product was purified by recrystallization method.

Procedure Synthesis of Substituted Phenylthiourea'

A) Nitro substituted phenylthiourea:

➢ Added□Weigh (0.1 mol) P-Nitro aniline, (0.1mol) Ammonium Thiocyanate; few ml Conc.Hcl (2ml) and 5 ml of water.

➢ Heated on Water bath at 100°C.

➢ Transferred in cold water.

➢ Separated By filtration.

➢ Dry it and recrystallized with ethanol.

➢ Melting Point; -145℃-150℃.

B) Bromo substituted phenylthiourea:

➢ Weigh (0.1 mol) P- Bromo Added few ml□aniline, (0.1mol) Ammonium Thiocyanate; Conc. Hcl (2ml) and 5 ml of water.

➢ Heated on Water bath at 100°C.

➢ Transferred in cold water.

➢ Seperated By filtration.

➢ Dry it and recrystallized with ethanol.

➢ Melting Point; -145℃-150℃.

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C) Nitro substituted phenylthiourea:➢ Weigh (0.1 mol) P-Chloro aniline, (0.1mol) Ammonium Thiocyanate; ➢ Added few ml Conc.Hcl (2ml) and 5 ml of water.

➢ Heated on Water bath at 100°C.

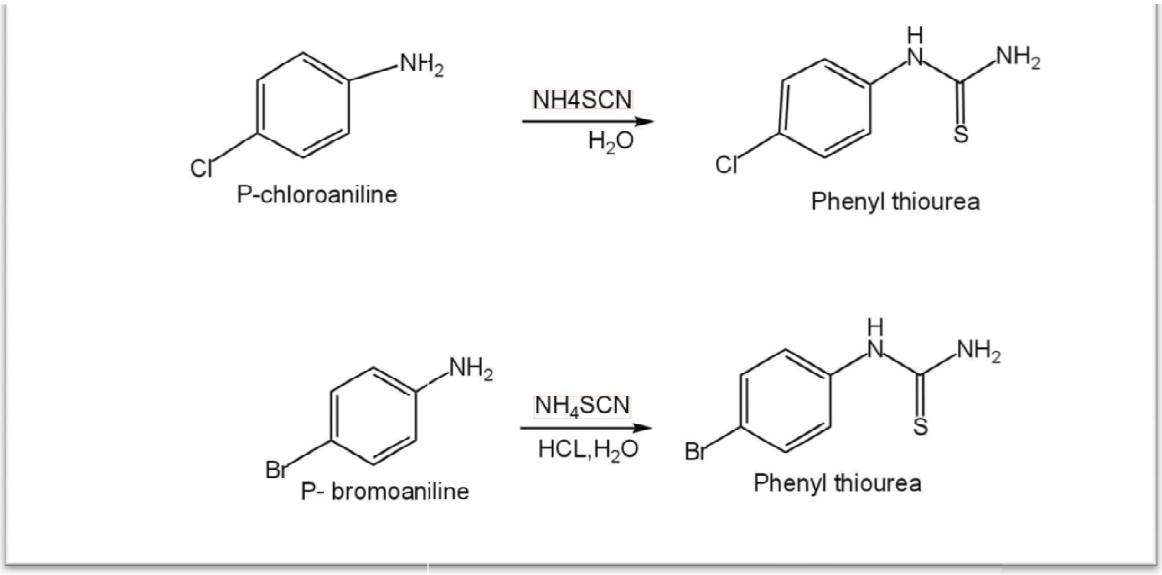
➢ Transferred in cold water.

➢ Separated by filtration.

➢ Dry it and recrystallized with ethanol.

➢ Melting Point; -145℃-150℃.

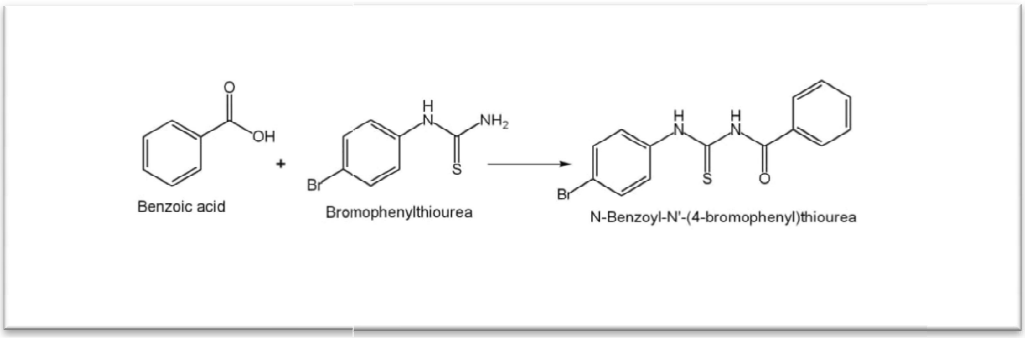
Reaction:



Newly synthesized of benzoic acid and phenylthiourea derivative:

1. Phenylthiourea (0.01mol) and Benzoic acid (0.01mol) was taken into the 100ml RBF.
2. The reaction was carried out in ethanol with catalytic amount of glacial acetic acid in Microwave assisted assembly.
3. After completion of the reaction, obtained solid product was filtered and purified by Recrystallization from ethanol.

Reaction:



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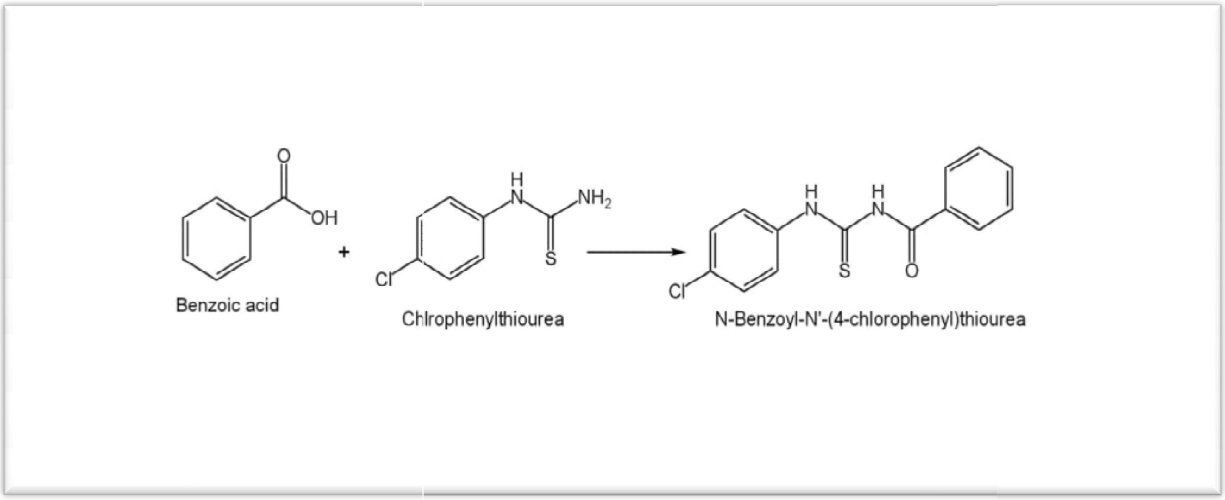

Compound	IUPAC Name	Molecular weight	Melting point
Compound A	N-Benzoyl-N'-(4 bromophenyl) thiourea	333 g/mol	170 ℃
Compound B	N-Benzoyl-N'-(4 Chlorophenyl) thiourea	290 g/mol	150 ℃

Table: Synthesized derivatives

SWISS ADME:

Compound Name	Molecular weight	H-Bonding acceptor	H- Bond Donors	Log p	Violations of Lipinski rule
N-Benzoyl-N'-(4 bromophenyl) thiourea	333 g/mol	1	2	2.93	0 Violation
N-Benzoyl-N'-(4 Chlorophenyl) thiourea	290 g/mol	1	2	2.80	0 Violation

CHARACTERIZATION:

FTIR

Fourier Transform Infrared Spectroscopy (FTIR) is a widely used analytical technique That provides valuable information about the chemical composition and structure Materials. It is a non-destructive technique that works by measuring the interaction between a sample and infrared radiation. FTIR is commonly used in a variety of Fields, including chemistry, materials science, pharmaceuticals, and forensic science. FTIR Works by shining an infrared beam

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of light through a sample, and measuring the intensity of the light that is absorbed by the sample at different wavelengths. This absorption Spectrum provides information about the chemical bonds present in the sample, which can be used to identify functional groups and determine the chemical composition of the material.

The resulting spectrum is a plot of the intensity of light absorbed by the sample as a function of wavelength, which is referred to as an infrared spectrum.

FTIR can be used to analyze a wide range of samples, including gases, liquids

Solids and powders. It is a powerful tool for identifying unknown compounds, monitoring chemical reactions, and characterizing materials. The technique is relatively fast, non-applications. overall, FTIR spectroscopy is a valuable analytical technique that provides important information about the chemical composition and structure of materials. applications makes it an essential tool in many fields, an essential tool in many fields, and its ease of use and reliability make it a popular choice among researchers and practitioners.

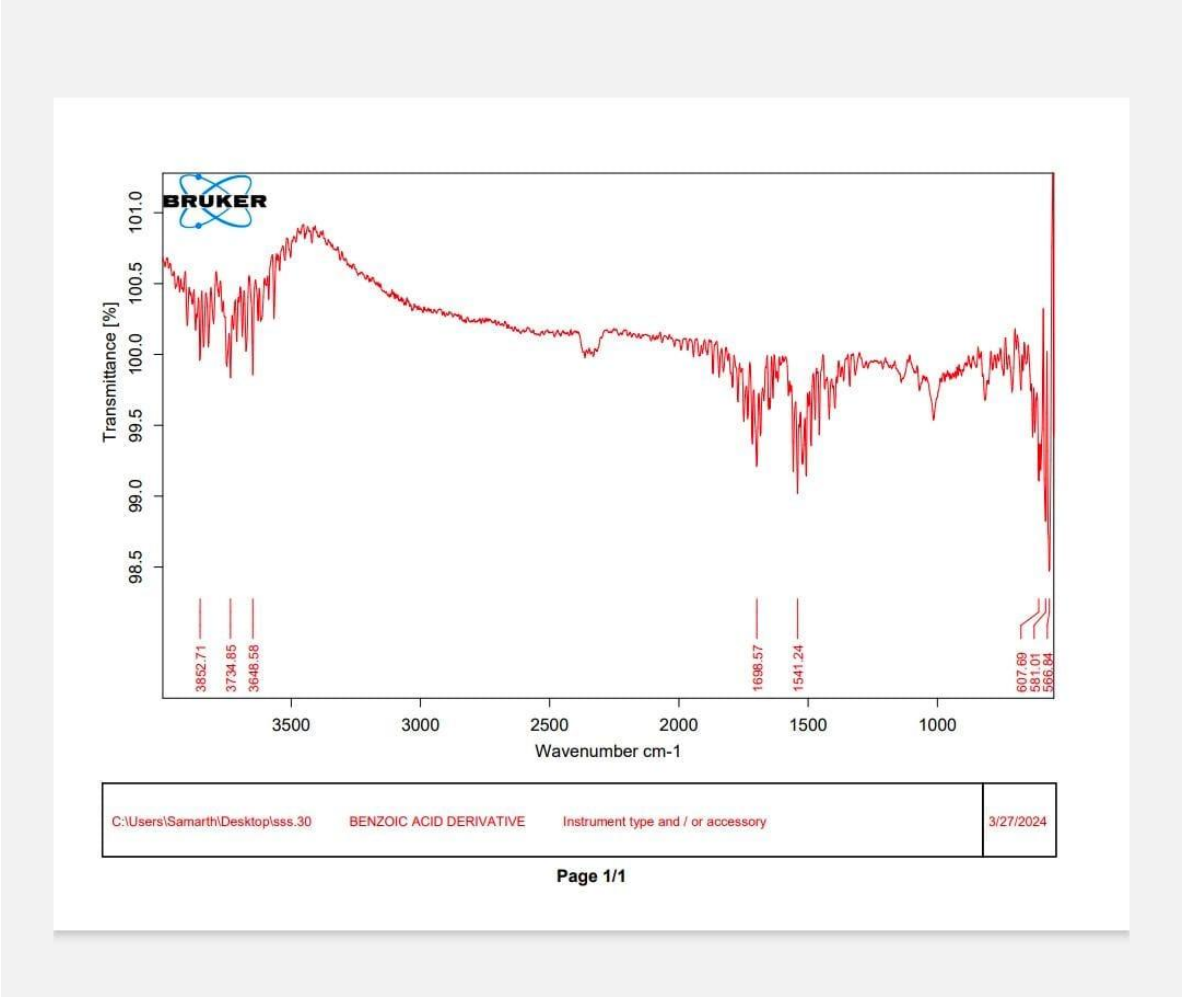

Fig. FTIR Benzoic acid derivative

NMR Spectroscopy:

Nuclear Magnetic Resonance (NMR) is a powerful analytical technique used to investigate the structure, composition, and dynamics of molecules. NMR is based on the interaction between atomic nuclei and a strong magnetic field and radiofrequency radiation. It is widely used in various fields, including chemistry, biochemistry, materials science, and

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medicine. In NMR, a sample is placed in a strong magnetic field and then subjected to radiofrequency radiation. The nuclei in the sample absorb and re-emit the radiation at a characteristic frequency, which depends on the local environment of the nucleus. By detecting the frequency of the emitted radiation, NMR can provide detailed information about the molecular structure and composition of the sample.

NMR can provide a wealth of information about a sample, including the number and types of atoms, the chemical environment of each atom, and the connectivity of atoms within a molecule. This information can be used to determine the identity of unknown compounds, monitor chemical reactions, and study molecular dynamics.

The NMR technique is often used in combination with other analytical techniques, such as mass spectroscopy and infrared spectroscopy, to provide a more picture of the sample. The most commonly used NMR technique is proton NMR, which is sensitive to the behavior of hydrogen atoms in the sample. Other nuclei, such as carbon-13 and nitrogen-15, can also be studied using NMR

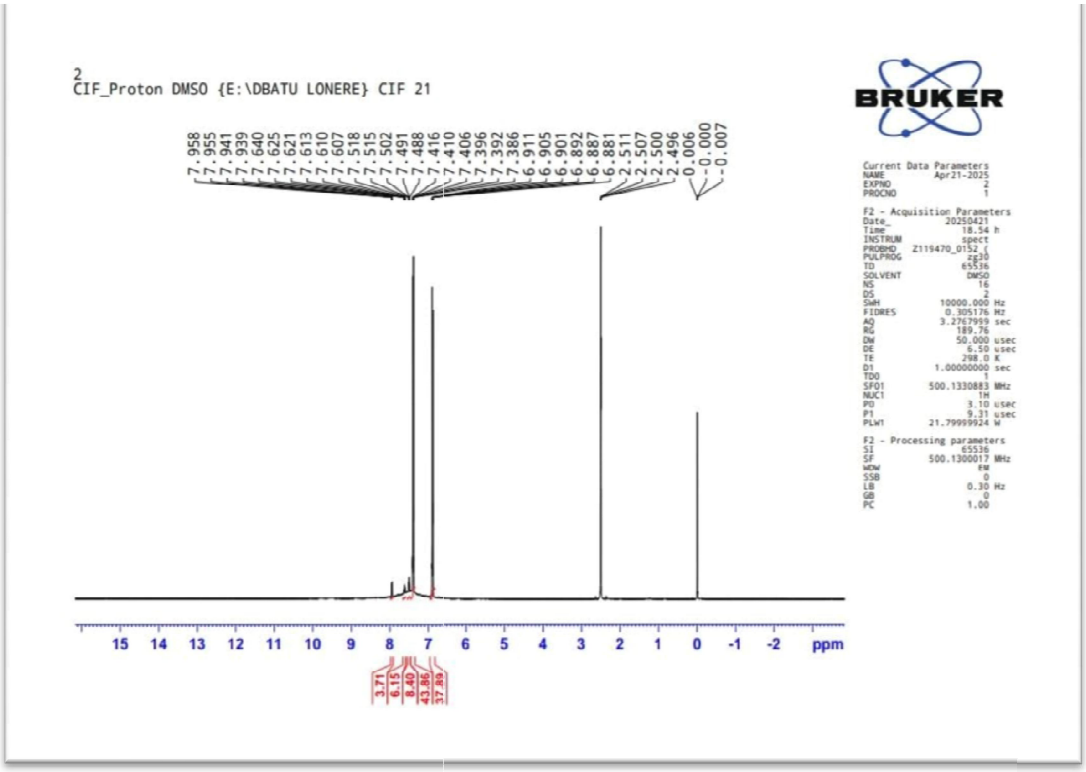

Fig: NMR Spectroscopy of Benzoic acid

CHROMATOGRAPHIC ANALYSIS:

Thin layer chromatography (TLC) is a type of chromatography used to separate and identify different components of a mixture. It involves placing a small spot of the sample on a thin layer of adsorbent material, such as silica gel or alumina, which is coated on a glass or plastic plate. The plate is then placed in a solvent, which travels up the plate by capillary action, carrying the components of the sample along with it. As the solvent moves up the plate, the different components of the sample are separated based on their affinity for the adsorbent material and the solvent. Components that have a strong affinity for the adsorbent material will move more slowly up the plate, while those with a weaker affinity will move faster. This results in the compo of the sample separating out into distinct bands or spots on the plate. Once the separation is complete, the plate is removed from the solvent and dried. The spots or bands can then be visualized using various techniques, such as staining with a chemical reagent or exposing the plate to UV light. The Rf value, or retardation factor, can be calculated for each component, which is the ratio of the distance traveled by the

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component to the distance traveled by the solvent. The Rf value is a characteristic property of a compound and can be used to identify unknown compounds by comparing their Rf values to those of known compounds. Silica gel G acted as stationary phase whereas the following solvent systems were used as mobile phase.

Chloroform: Methanol (9:1)

Fig. A :- TLC Plate Of Benzoic acid And Bromophenyl thiourea.

Fig. B :- TLC Plate Of Benzoic acid And chlorophenyl thiourea.

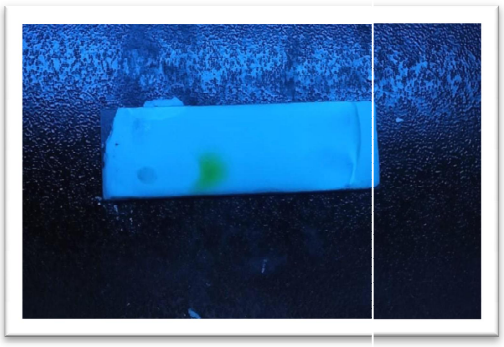

Fig: A

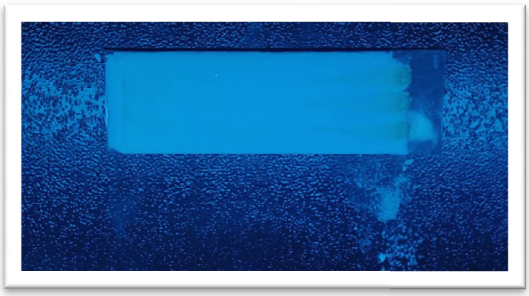

Fig: B

The Rf value is the ratio of the distance traveled by the component to the distance traveled by the solvent front. This value is characteristic of each component and can be used to identify the components of the mixture.

$$\text{Retention Factor (RF)} = \frac{\text{Distance travelled by the component}}{\text{Distance travelled by the solvent.}}$$

The retention factors are as follows:

Sr.	Figure	Rf Value
1	Fig A	0.76
2	Fig B	0.80

BIOLOGICAL ACTIVITY:

Liquid dilution method or Test tube method

Use a series of test tubes which contain a double-strength medium and are labelled as Test tube numbers. In the first tube (un-inoculated), inoculum is not added which is used for checking the sterility of the medium. All other in a eleven test tubes, inoculum (3 to 4 drops) is added to reach the final concentration of microorganisms is 10 to 10 cells/ml. In all test tubes, test chemical is added ranging from 0.5 to 5 ml except in the control tube. The second tube (control) is used to check the suitability of the medium for growth of the test microorganism and the viability of the inoculum. The final volume min all test tubes is adjusted by using sterile water. The contents of all test tubes a properly mixed and incubated at 37°C for 2 to 3 days. After incubation, all test tubes an examined for the growth in the form of turbidity and the results are recorded and minim inhibitory concentration is calculated. It is also necessary to conduct a preliminary experiment to determine the approximate range (test solution) which would be suitable the test.

Antimicrobial Activity:

The inhibition zone diameter of all synthesized compounds was determined through the cup-plate agar diffusion method to evaluate their in vitro antimicrobial activity against *Salmonella typhi* using benzoic acid derivative product dissolved in methanol and placed in right side cup as a test and methanol as control in left side cup. A clear ring surrounding the antimicrobial source where bacterial growth is prevented.

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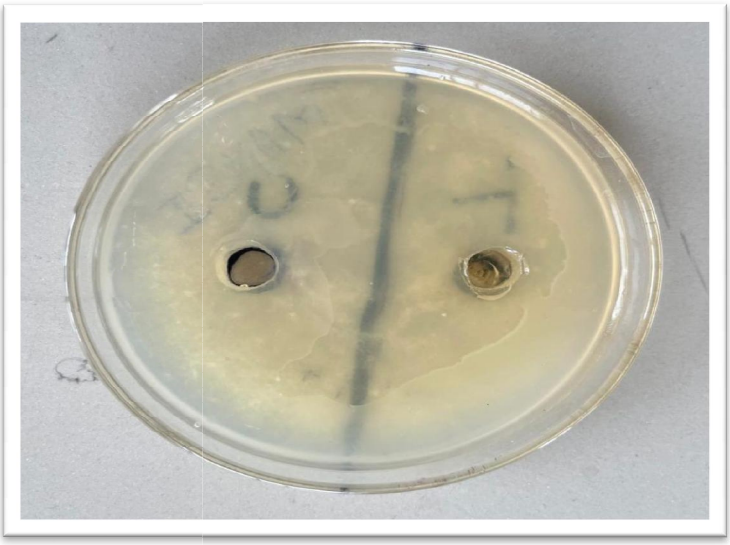

Fig: Antimicrobial Screening

RESULT:

Phenylthiourea derivatives were prepared from the substituted aromatic amines which in the presence of ammonium thiocyanate forms substituted 1-phenylthiourea in acidic medium. This substituted phenylthiourea condensed into benzoic acid in the presence glacial acetic acid and ethanol obtained 2,4,5-triphenyl imidazole and phenylthiourea derivative. All the compounds obtained were good yield ranging from 70- 75%. The homogeneity of the compounds was monitored by performing TLC by which Rf values were calculated. The solvent system used for all the compounds was Chloroform: Methanol (9:1). The antimicrobial activity of the test drug against Salmonella typhi s ranged from 0.5 to 50 µg/ml.

II. CONCLUSION

The fundamental goal of medicinal chemistry is the development of new anti microbial therapeutic agents. In conclusion, synthesis, characterization, and pharmacological activity of newly synthesized derivatives of phenylthiourea are promising areas of research with a wide range of potential applications in the fields of organic chemistry and drug discovery. synthesis has been shown to be a rapid and efficient method for synthesizing new compounds, while characterization techniques such as FT-IR, 1H-NMR, and mass spectroscopy can provide valuable information on the molecular structure and purity of the synthesized compounds. The evaluation of antimicrobial activity is essential in the development of new drugs and antibiotics, and the discovery of new antimicrobial agents is critical in the fight against infectious diseases. The evaluation of antimicrobial activity showed that some of the synthesized compounds had promising activity against a range of microorganisms. Overall, this research contributes to the growing body of literature on the

use of microwave-assisted synthesis in the field of organic chemistry and provides valuable insights into the structure-activity relationship of newly synthesized derivatives of phenylthiourea. Further research is needed to explore the potential applications of these compounds in the development of new drugs and antibiotics, as well as to investigate other areas of research where microwave-assisted synthesis can be applied.

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