SYNTHESIS CHARACTERIZATION AND ANTIMICROBIAL EVALUATION OF BENZIMIDAZOLE DERIVATIVES

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Abstract :

This study focuses on the synthesis and evaluation of 2-substituted benzimidazole derivatives ` their potential antibacterial activity. Medicinal chemistry plays a crucial role in drug discovery and development, especially through the synthesis of heterocyclic compounds like benzimidazole, known for diverse biological activities. The synthesized compounds were characterized using physicochemical tests and IR spectroscopy. Antibacterial evaluation was conducted against Staphylococcus aureus and Escherichia coli, using ciprofloxacin as a standard. The results showed that the synthesized compounds exhibited moderate antibacterial activity, supporting their potential as lead molecules for further therapeutic development.

Keywords :

Medicinal chemistry, Drug discovery, Drug development, Structure-activity relationship (SAR), Lead compound modification, Pharmacological profiling, Receptor binding Enzyme inhibition

INTRODUCTION

Medicinal chemistry

The discipline of medicinal chemistry leads to the discovery and development of new agent for treating diseases. Most of the activity is directed to new natural or synthetic organic compounds.[1]

Medicinal chemistry deals with the discovery, development, identification and interpretation of the mode of action of biologically active compounds Add the molecular level. It is also concerned with the study, identification and synthesis off the metabolic products of drug and related compounds[2]

It involves isolation off compound from the natural or synthesis off the new molecules, Investigation of the relationships between the structure of natural synthetic compound And their biological activities, Elucidation of their interactions with receptors of various kinds, Including enzyme and DNA, The determination of their adsorption, transport, Distributary properties and studies of the metabolic transformation of this chemicals into other chemical and their excretion.[3]

It deals with the discovery and design of new therapeutic chemicals and their development into useful medicines and the forefront of innovation, Blending of synthetic chemistry, molecular modeling, And pharmacological studies to discover design new drugs and to investigation their interaction at the molecular, cellular and animal level. Medicinal chemist have a greater role in development of numerous organic compounds suitable for treatment of illness and maintenance and field of human beings.[4]

Drug discovery

Drug discovery is process of designing and synthesizing new compound and evaluating to assess drug safety and efficacy in humans. The traditional way to discover new drugs has been to screen a large number of synthetic chemical compound or natural product or desirable effects. Modification of lead compounds are often carried out to improve activity, Reduce side effects and to improve performance.[5]

Synthesis

Chemical synthesis is the preparation of a compound, usually an organic compound which repaired or synthesized by performing various chemical reactions using an In expensive starting material and changing its molecular structure, By reaction with other chemicals. The best chemical synthesis are those that use cheap starting materials which requires only a few steps, And have a good output of product based on amounts of starting chemicals[7]

Importance of heterocycles in medicinal chemistry

Heterocycles are organic compounds containing at least one atom of carbon and at least one element other than carbon such as sulfur, Oxygen or nitrogen with a ring structure. It is one of the vital classes of organic compounds which are used to mainly biological fields due to its activity in multiple illness. Today there are lot of heterocyclic Compounds are known, Day by day due to their synthetic utility. Heterocycles have been found for key structural in medicinal chemistry and also they are frequently found in large percent in bio-molecules such as enzymes Natural products and biological active compound including antifungal, anti-inflammatory, antibacterial, anti oxidant, anti-convulsant, anti allergic, enzyme inhibitors, anti-diabetic, anti HIV, anti cancer activity. [8]

Benzimidazole

Benzimidazole is the heterocyclic compound form from benzene and imidazole ring containing nitrogen, Oxygen sulfur and its derivatives are of wide interest because of their diverse biological activity and clinical applications, They are remarkable effective compounds both with respect through their inhibitory activity and their favorable selectivity ratio. Reported nucleus is a constituent of vitamin - B12. Benzimidazole Are regarded as a promising class of bioactives heterocyclic compounds that exhibit a range of biological activities like anti microbial, anti viral, anti diabetic, anti cancer activity. Benzimidazoles Exhibit significant activity as potential antitumor agents, Smooth muscle cell proliferation inhibitors. Some of the important benzimidazole Derivatives have been reported as thyroid receptor agonists Gonadotropin releasing hormone receptor. The imidazole core core is a large number of natural products and pharmacologically active compounds. The synthesis of novel benzimidazole derivatives remain a main focus of medicinal research. The overview summarizes the chemistry of different derivative

of substituted benzimidazole along with their antimicrobial activity containing anti malarial, anti-fungal antibacterial, antiviral activities.

EXPERIMENTAL WORK

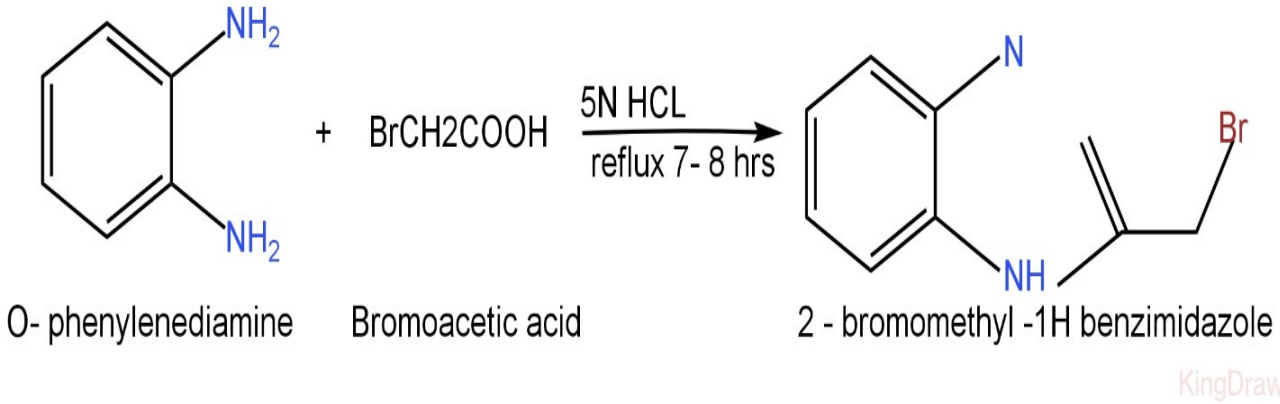
Material –

2-bromomethylbenzimidazole, m-nitro aniline, potassium iodide, ethanol, potassium hydroxide.

Step – 1:

A mixture of o-phenylenediamine (0.1mol) and monobromoacetic acid (0.1kol) was refluxed for 3h in 4N hydrochloric acid (50ml) on a water bath. The reaction mixture was cooled and basified with ammonium hydroxide solutionThe precipitate thus obtained was dried and recrystalized From methanol with activated charcoal treatment. The pure product obtained was a slightly yellow colored crystal Whose melting point was 152 -152°C and the yield was 89%.

Step 1- proposed reaction

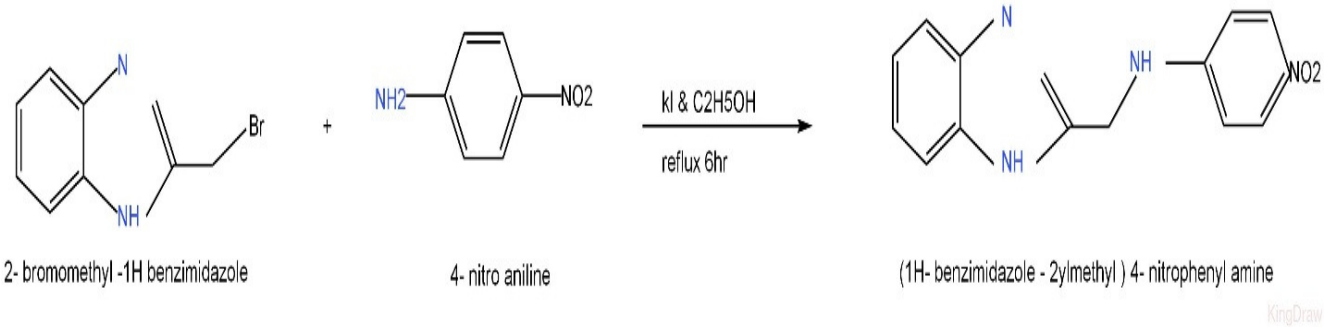


Step- 2:

A mixture of 2- bromomethyle benzimidazole (0.10mol), substituted primary aromatic amine (0.01mol) and kl (0.01mol) in 50ml of ethanol was heated under reflux for 6h, KOH (0.01mol in 5 ml of water) was added with continuous stirring for 2h. Finally the reaction mixture was left

aside at room temperature and then poured into crushed ice. the solid product precipitated was filtered off, Recrystallized from ethanol and dried in vacuum desiccators.

Proposed reaction ;



RESULTS AND DISCUSSION

The compounds were evaluated in vitro antibacterial activity against staphylococcus aureus and Escherichia coli Using ciprofloxacin as standard. The zone of inhibition of the synthesized compounds against staphylococcus aureus, and Escherichia coli Is presented in table.

Figure 1: Antimicrobial evaluation

Data of antimicrobial activity of synthesized compound:

Sr.No	Compound	Zone of inhibition in (mm)	
		Staphylococcus aureus	Escherichia coli
1	RB-4	09	11
2	Ciprofloxacin	25	24

Physicochemical characterization for 2- bromomethyle benzimidazole

PHYSICAL PROPERTIES :

Sr.No.	Test	Observation
a.	Colour	Brick red Colour
b.	Odour	Characteristic

SOLUBILITY:

Sr. No.	Test	Observation
a.	Water	Soluble
b.	Hydrochloric acid	Soluble
c.	Sulphuric acid	Soluble
d.	Sodium hydroxide	Practically soluble
e.	Acetone	Soluble
f.	Ether	Soluble

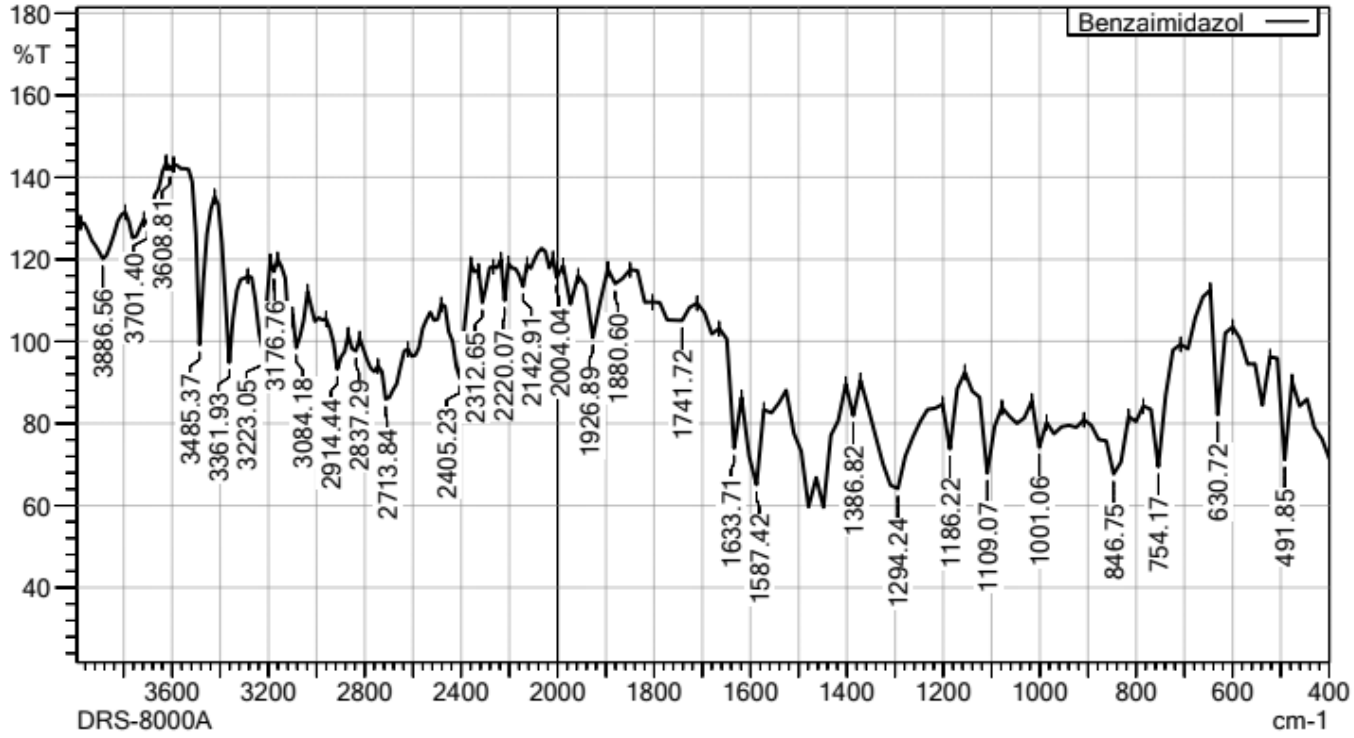
ELEMENT DETECTION:

Sr.No.	Test	Observation	Inference
a.	**Nitrogen –** 2-3 ml of sodium fusion extract into a clean test tube, 0.1-0.2g of powdered iron sulphate crystals was added.The mixture was heated to boil and cooled. To this, dilute H_2SO_4 was added to dissolve the iron hydroxide	Prussian blue precipitate was observed	Nitrogen was found to be present
b.	**Sulfur –** 2ml of sodium fusion extract, dilute acetic acid was, added and few drops of lead acetate solution was added	Black precipitate of lead sulphide wasnot developed	Sulphur was found to be absent.

MELTING POINT:

Melting point was found to be 176-178°C

IR spectroscopy of synthesized compound:



Sr.No.	Functional group	2-bromomethylbenzimidazole ranges
1.	N-H	3395
2.	C-H(CH2)	3057.23
3.	C=C(Ar)	842
4.	C=N	1323
5.	NO2	1410
6.	Ar ring	923.92

ANTIMICROBIAL EVALUATION

Antimicrobial activity:

The antibacterial activity of newly synthesized compounds was evaluated against gram positive bacteria i.e. staphylococcus aureus and gram negative bacteria i.e. Escherichia coli. Ciprofloxacin was used as a standard drug.

Preparation of nutrient agar medium

Sr. No.	Ingredients	Quantity taken
1.	Peptic digest of animal tissue	5gm
2.	Sodium chloride	5gm
3.	Beef extract	1.50gm
4.	Yeast extract	1.50gn
5.	Agar	15gm
6.	Distilled water	1000ml

All the ingredients were dissolved in distilled water, adjust the ph to 8.0-8.4 with 5M NaOH solution and boil for 10-15 min. filtered the solution. Adjust the ph of the medium by 7.4±0.2 by the addition of dil. HCl sterilized the medium in autoclave for 15min. At 121°C.

Preparation of test solution:

The solution of the various benzimidazole derivatives in concentration of 100µg was prepared in DMSO.

Preparation of standard solution:

Weigh 10mg of standard drug and diluted to 10ml to from 1000µg/ml of stock solution from this stock solution, we took 1ml and diluted to 10ml to form 100µg/kl of standard solution.

Procedure:

Inoculate previously liquefied sodium appropriate to assay with quantity of suspension of the microorganisms. Add the suspension to the medium add temperature 40 to 50°C and immediately pour the inoculated Medium into Petri dishes to give a depth of three to four minute ensures that the layer of the medium are uniform in thickness by placing the dishes on the level of surface. made few cavities on the surface of medium. Pour the solution Off non concentration of the standard preparation and taste preparation to cavities by means of micropipette in a sterile condition. Leave the dishes Standing for one to four hours in refrigerator as appropriate as a period of pre incubation diffusion to minimize the effects of variation in time between the applications of different solution. Incubate them for about 24 hours at the temperature indicated accurately measured the diameter of zone of inhibition.

Conclusion:

The synthesized benzimidazole derivatives demonstrated moderate antimicrobial activity. While not exhibiting the potency of the standard drugs used in the study, the compounds showed a discernible inhibitory effect against the tested microorganisms. This suggests that the benzimidazole scaffold holds promise for further development as a potential source of new antimicrobial agents. Future research should focus on structural modifications aimed at enhancing the activity and selectivity of these compounds. Additionally, further studies to elucidate the mechanism of action of these derivatives are warranted.

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