https://doi.org/ 10.33472/AFJBS.6.Si2.2024.594-601

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF BENZIMIDAZOLE DERIVATIVES

Mrunal Raut[1], Tejal Rahane[2], Monika Ranjane[3], Sonal Kakade[4], Ganesh Y. Dama[5], Kiran C. Mahajan[6]

[1,2,3,4]Department of Pharmaceutical Chemistry, SGMSPM's Sharadchandra Pawar College of Pharmacy, Dumbarwadi(otur), Tal-Junnar, Dist- Pune, Maharashtra, India, 410504

[5]Department of Pharmacognosy, SGMSPM's Sharadchandra Pawar College of Pharmacy, Dumbarwadi(otur), Tal-Junnar, Dist- Pune, Maharashtra, India, 410504.

[6]Department of Pharmaceutics, SGMSPM's Sharadchandra Pawar College of Pharmacy, Dumbarwadi(otur), Tal-Junnar, Dist- Pune, Maharashtra, India, 410504.

Corresponding Email: [1*]mrunalraut157@gmail.com

Article History

Volume 6,Issue Si2, 2024

Received:10 Mar 2024

Accepted : 08 Apr 2024

doi: 10.33472/AFJBS.6.Si2.2024.594-601

Abstract:

In the medical field Benzimidazole derivatives plays important role and have various pharmacological effects such as antibacterial, antiviral, anticancer, and antidiabetic. The effectiveness of these clinically helpful drugs in treating microbial infections and other activities has support the development of some more effective and important compounds. These are very potent compounds. Large pharmacological and biochemical studies have demonstrated the effectiveness of these molecules against a variety of microbial strains. This review is concluded to learn more about the chemical properties of various derivatives of these substituents and their pharmacological activities.The synthesized compound's structure was assessed using spectroscopic and elemental analytical techniques. The bactericidal activity of every produced molecule was evaluated. With regard to Gram-positive bacteria, all derivatives exhibited strong activity, while their effects against Gram-negative bacteria were minimal.

Key words: Benzimidazole, antimicrobial activity, pharmacological activites, spectroscopy, bacteria

Introduction:

Salmonella typhimurium, *Escherichia coli*, *Staphylococcus aureus*, and *Streptococcuspyrogenes*are only a few of the parasite bacteria that significantly affect human mucosal health. *Serratia*, *Salmonella pyrogenes*, *Salmonella typhimurium*, and *Escherichia coli* infections can cause severe tissue damage in the host and potentially fatal diseases.

Millions of individuals in impoverished nations are susceptible to food poisoning, rheumatic fever, and diarrhoea due to these bacterial parasites. "More than 50 million people around the world are infected each year, and up to 110,000 of them die." The most often prescribed medications to treat this bacterial infection are amoxicillin, norfloxacin, and ciprofloxacin; nevertheless, they can have harmful side effects[1].

Benzimidazole represents a class of nitrogen heterocyclic compounds with biological and pharmacological activity. Heterocyclic compounds synthesized by organic chemists are used as drugs, dyes, and agricultural chemicals, and are becoming increasingly important in adhesives, molecular engineering, polymers, and many other fields. Naturally occurring heterocyclic units play crucial roles in biological processes. These are commonly found in nature in plant nucleic acids, alkaloids, anthocyanins and flavonoids, and chlorophyll. In addition, some proteins, hormones, and vitamins contain aromatic heterocyclic systems[4].

Therefore, we need to develop an innovative method for bioactive heterocycles in organic synthesis and medicinal chemistry that features easy operation, greener approach, simple post-processing, selectivity, higher yield, and high atom Economical and other advantages. Nitrogen.The relative frequency with which different nitrogen heterocyclic compounds are introduced into approved therapeutic structures was revealed by a recent analysis of the nitrogen heterocyclic composition of U.S. Food and therapeutic Administration (FDA)-approved pharmaceuticals.

Benzimidazole is an aromatic N-heterocycle, which is created by the combination of benzene's nitrogen-containing heterocycle and imidazole ring**.(Fig.1)** It is present in vitamins, proteins and nucleic acids[5].

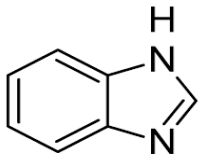

Fig.1: Structure of Benzimidazole

Benzimidazole derivatives continue to be a major focus of pharmaceutical research and exhibit. Antimicrobial activity that includes anti- viral, anti-bacterial, anti-malarial and anti-fungal activities.Antimicrobial agents kills microorganisms and stops their growth (bacteriostatic agent). When it comes to their excellent selectivity ratio and inhibitory activity, benzomidazoles are exceptionally powerful compounds. A class of bioactive heterocyclic compounds with a wide range of biological activity, benzomidazoles are thought to be promising. Specifically, this core is a component of vitamin B12.The health of the human mucosa is significantly impacted by versatile parasite bacteria such *Escherichia coli, S. aureus, S. pyrogenes,* and *Salmonella typhimurium. Staph infection, streptococcus pneumoniae, salmonella typhimurium,* and *Escherichia coli* infections can result in severe tissue damage and potentially fatal illnesses. Millions of individuals in developing nations suffer from food poisoning, rheumatic fever, and diarrhea due to these bacterial parasites[5].

Well-known biologically active N-contaningheterocycles with a range of biological activity reported are benzimidazoles and its equivalent. Owing to their significance in chemotherapeutics, numerous benzimidazoles compounds have been documented[7].

The Benzimidazoleand its derivatives exhibits pharmaceutical applications containing anti-virals, antifungals, anti-convulsants, anti-diabetics, antihypertensives. It also has application that includes Ligands, catalysts, fungisides, herbicides, pesticides, insecticides, optical sensing, medicinal chemistry, etc[9].

Materials and Methods:

Materials:

Chemicals:

Orthophenylenediamine was bought from Chemdyes corporation, Paraminoacetophenone was bought from Chemdyes corporation, Formaldehyde, Formic acid and ethanol was bought from Molychem.

Method of synthesis:

1) **Method of synthesis of Benzimidazole:**
   10 ml of 90% formic acid are added to a 250 ml round-bottom flask containing 2 gm of orthophenylenediamine. The combination above was heated for 2 hrs at 100°C in a water bath. When the combination is just alkaline to litmus (red to blue), cool it to room temperature and put it side by side in the ice bath. Slowly add 10% NaOH solution while rotating the mixture constantly. Filter the crude benzimidazole and wash with enough water[2].

Fig.2:Synthesized Benzimidazole

2) **Method of synthesis of 1-(4-((1H-benzimidazol-1-yl)methylamino) phenyl) ethanone derivatives:**
   In 40 ml of ethanol, 1.18 grams of benimidazole and 1.35 grams of p-aminoacetophenone were dissolved. 2.7 ml of formaldehyde was added to the solution above, and it was magnetically swirled for 3 hrs at room temperature. The final solution was then chilled in an ice bath after refluxing for an1 hour on a water bath. The resulting separated product was dried, filtered, and crystallized from ethanol[1].

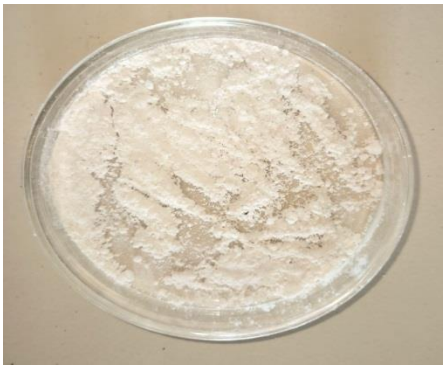

Fig..3: Synthesized 1-(4-((1H-benzimidazol-1-yl) methylamino) phenyl) ethanone

Evaluation:

1) **Color:**
   Benzimidazole itself may be a white to off-white compound. However, when their derivatives are synthesized, their color may change depending on the specific chemical modification.
2) **Odor:**
   The white color is due to its crystal structure or the presence of certain functional groups. It is an odorless white crystalline powder. The smell of a derivative can vary greatly depending on its specific chemical structure and any functional groups attached to its core. Although generally odorless, the addition of certain substituents can impart different odors to these derivatives.
3) **Solubility:**
   Procedure: Solubility experiments were carried out in a test tube 0.25 gm of solid sample was added to 0.5 ml of distilled water and lightly tap the tube with the use of glass stirring rod.
4) **Melting point:**
   Procedure: In the melting point apparatus a small amount of the sample is placed in the capillary tube which contains the paraffin oil, gradually heated and observed the temperature at which drug melts. Positive identification is considered for these drug when the temperature of these drug falls within the 145-147^{o}C range.
5) **Reaction with acids:**
   Benzimidazole reacts with such as hydrochloric acid to form water-soluble salts.
6) **Ultraviolet Spectroscopy:**
   Turn on the ultraviolet spectrophotometer and let it warm up. Changing the range of wavelengths and the width of slits, as necessary for the experiment, Transfer the sample solution to a fresh cuvette and place it in the spectrophotometer. Keep track of the absorption of the sample at a specific wavelength or over a range of wavelengths.
7) **Infrared spectroscopy:**
   Prepare samples containing molecules of interest. It can be in liquid, solid or gas form.
   Place the sample into the infrared spectrometer. The instrument emits infrared radiation within a certain frequency range. Infrared radiation interacts with sample molecules. Molecules absorb infrared light at specific frequencies that correspond to the vibrational modes of the functional groups present in the molecule. The instrument records the amount of infrared radiation absorbed at each frequency. This data is then recorded as an infrared spectrum, with peaks corresponding to absorption frequencies.
8) **Minimum Inhibitory Concentration (MIC) test:**
   Add 1 gm peptone, 1 gm of beef extract, 2 gm of agar, 0.5 gm of sodium chloride in 100 ml of distilled water. Heat the mixture and stir until all ingredients are completely dissolved. The dissolved mixture was autoclaved at 121°C for 15 min. After autoclaving, allow the culture to cool but not solidify. Pour nutrient agar into each plate and place the plate on a sterile surface until the agar solidifies. Place a lid on each Petri dish and store the Petri dishes in the refrigerator. Using sterile loop inoculate the standard amount of microbial culture on petri dish, then place the plate in the incubator at 100^{o}C for 24 hours.

After that, each 0.2, 0.4, 0.6, 0.8 concentration of Benzimidazole derivative was pour into the holes on petri plate and then place it in incubator for 24 hours. Observed the results of petri plate by using colony counting method.

Result and discussion:

1) Organoleptic properties:

Table no. 1: Organoleptic Properties of Benzimidazole derivatives

Parameter	**Result**
Color	White to off white
Odor	Characteristic
Texture	Crystalline

2) Solubility:

Solubility of Benzimidazole derivatives was determined and given in table no.1

Table no.2: Solubility of Benzimidazole derivatives

Solvent	**Solubility**
Ethanol	Soluble
Methanol	Soluble
Diethyl ether	Sparingly soluble
Water	Slightly soluble
Chloroform	Soluble
Benzene	Sparingly soluble

Benzimidazole is slightly soluble in water and easily soluble in organic solvents such as methanol, chloroform, and ethanol. It is sparingly soluble in benzene, diethyl ether.

3) Melting point:

The melting point of Benzimidazole derivative is about 145-147°C, which can be determined experimentally. The average mean of the Benzimidazole derivative M.P. was found to be 146^0C.

4) Ultraviolet Spectroscopy:

As per the Lambert'sand Beer's law, the concentration increases with the increasing absorbance. Ultraviolet Spectroscopy of Benzimidazole derivatives was determined andgiven in table no.3. and fig.4.

Table no.3: Benzimidazole derivatives at different concentration

Sr.no	**Concentration ((µg/ml)**	**Absorbance**
1	0	0

2	20	0.0361
3	30	0.0494
4	40	0.0639
5	50	0.0789

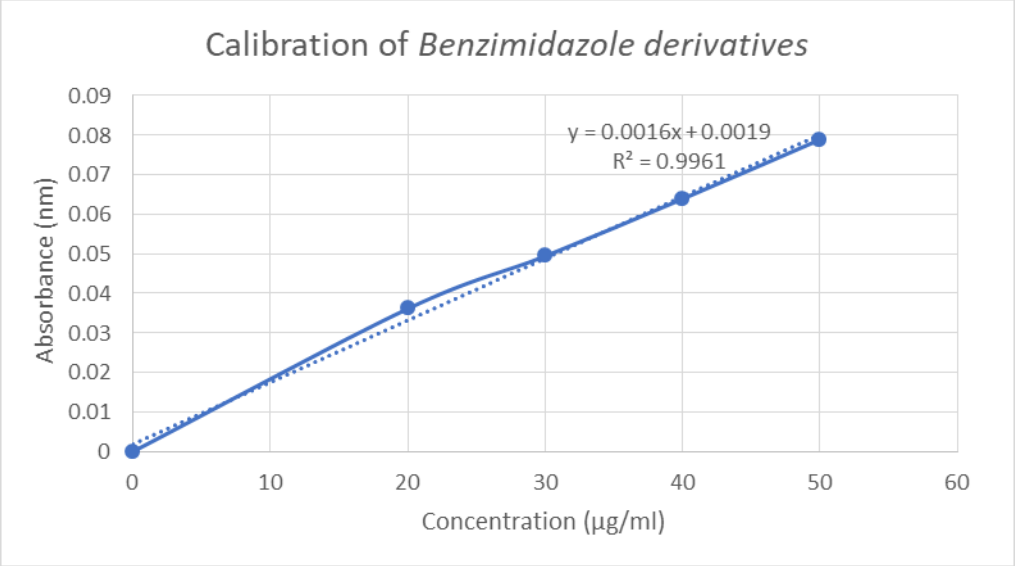

Fig. 4: Calibration curve of Benzimidazole derivatives

UV spectroscopy of a derivative measures the absorption of light in the UV range by a solution of the derivative. The UV spectrum of a derivative can be used to determine its electronic properties and identify the molecule.

5) Infrared Spectroscopy:

Infrared Spectroscopy of Benzimidazole derivatives was determined and given in the fig.5

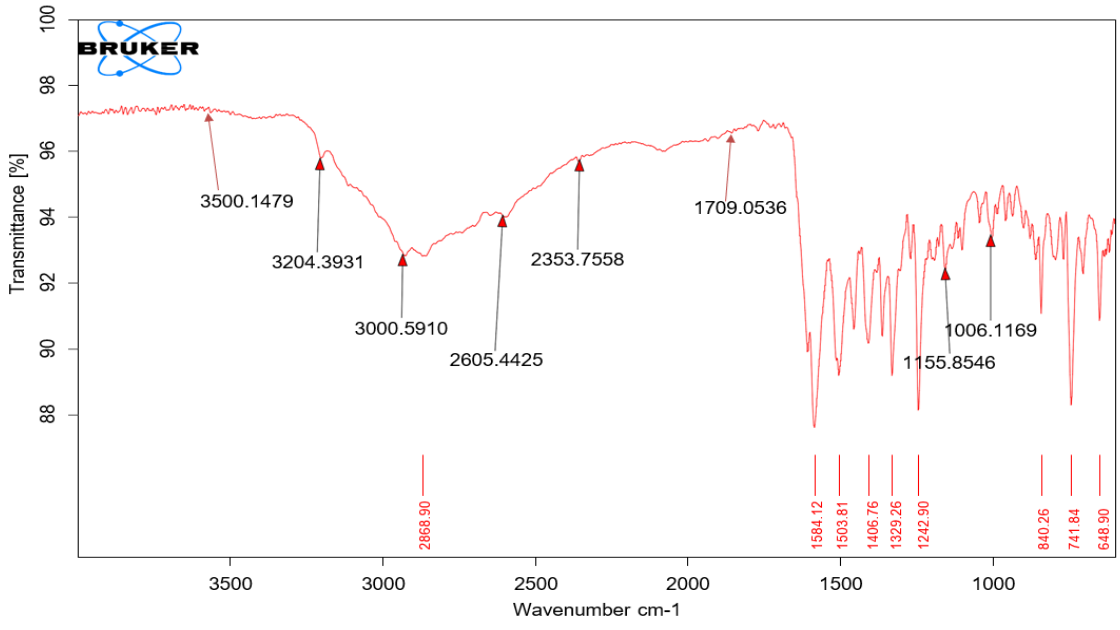

Fig.5: IR peak of Benzimidazole Derivatives

In the infrared (IR) spectrum of benzimidazole derivatives, one usually expects peaks representing the following functional groups: B . Corresponding C-H stretch (approximately 3100-3000 cm^-1), C=C stretch (approximately 1600–1450 cm^-1) and C=N stretching (about 1600-1680 cm^-1) possibly some peaks indicating the presence of aromatic rings. Specific peaks may vary depending on substitution patterns and other factors.

6) Minimum Inhibitory Concentration (MIC) test:

Minimum Inhibitory Concentrationof Benzimidazole derivatives was determined and given in the table no.4 and fig.6 :

Table no.4: Benzimidazole derivatives at different concentration

Concentration (µg/ ml)	**Diameter of zone of inhibition(cm)**
0.2	0.1
0.4	0.4
0.6	0.7
0.8	1

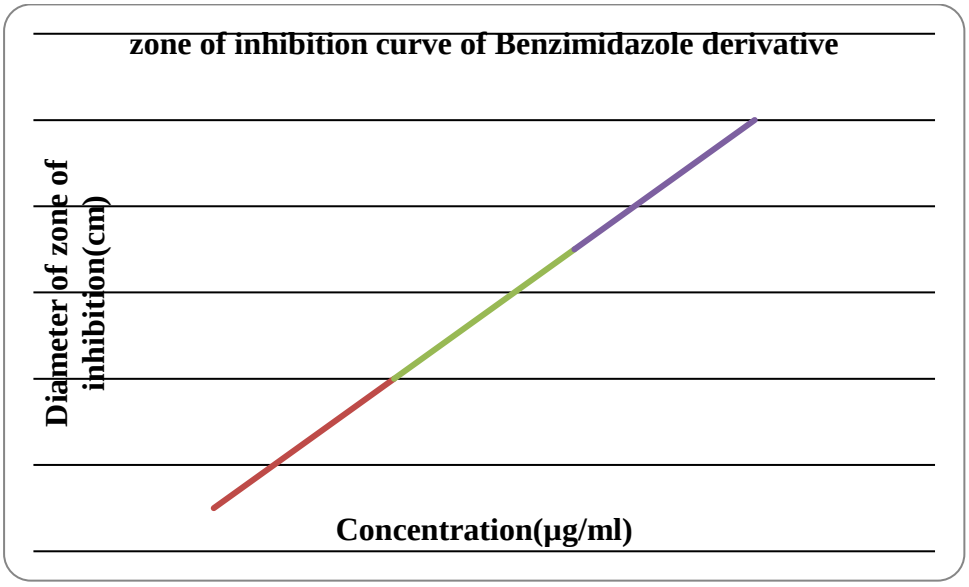

Fig.no.6: Zone of inhibition curve of Benzimidazole derivatives

Conclusion:

By using a multi-step reaction synthesis to create a series of novel benzimidazoles from o-phenylenediamine, an efficient antibacterial agent was developed. These compounds were then characterized by FT-IR and UV analysis. The agar streak dilution method was used to screen the title chemical for its in vitro antibacterial activity, and its minimum inhibitory concentration (MIC) was calculated against various strains of microorganisms. This substance can therefore function as a lead molecule for an antibacterial drug that is clinically beneficial. Because its heterocyclic core is important for synthetic and medicinal purposes,

the synthesis of benzimidazole derivative has long been a flourishing field and remains an active field from both an academic and industrial perspective. Overall, this review helps identify potential futures. Looking for directions to develop new effective benzimidazole

derivatives through greener approaches and targeting various biological targets.

Acknowledgment:

The authors are very thankful to Department of chemistry and principal for providing that support and facility to furnish our task.

Conflict of interest:

The authors declare no conflict of interest.

Author's contribution:

We declare that this work was created by the author named in this article and that all liability related to claims related to the content of this article rests with the author.

Financial support:

The authors have no financial support for the study.

References:

1) Krishnanjaneyulu IS, Saravanan G, Vamsi J, Supriya P, Bhavana JU, Kumar MV. Synthesis, characterization and antimicrobial activity of some novel benzimidazole derivatives, Journal of advanced pharmaceutical technology & research, 2014 ;5(1):21-7.
2) Furniss BS, editor. Vogel's textbook of practical organic chemistry Pearson Education India; 2011:1162.
3) Klimešová V, Kočí J, Pour M, Stachel J, Waisser K, Kaustová J. Synthesis and preliminary evaluation of benzimidazole derivatives as antimicrobial agents, European journal of medicinal chemistry, 2002;37(5):409-18.
4) Mishra AK, Gautam V, Gupta A, Bansal R, Bansal P, Kumar S, Gupta V, Synthesis and antimicrobial activity of some newer benzimidazole derivatives–an overview. Journal of Pharmacy Research 2010;3(2):371-8.
5) Ansari KF, Lal C. Synthesis, physicochemical properties and antimicrobial activity of some new benzimidazole derivatives, European journal of medicinal chemistry, 2009 ;44(10):4028-33.
6) El-masry AH, Fahmy HH, Ali Abdelwahed SH. Synthesis and antimicrobial activity of some new benzimidazole derivatives, molecules. 2000 ;5(12):1429-38.
7) Reddy VB, Singla RK, Bhat VG, Shenoy GG. Synthesis and antimicrobial studies of some novel benzimidazole derivatives, Asian Journal of Research in Chemistry, 2009;2(2):162-7.
8) Ansari KF, Lal C. Synthesis and evaluation of some new benzimidazole derivatives as potential antimicrobial agents, European Journal of Medicinal Chemistry2009 ;44(5):2294-9.
9) Walia R, Hedaitullah M, Naaz SF, Iqbal K, Lamba HS,Benzimidazole derivatives–an overview, Int. J. Res. Pharm. Chem. 2011;1(3):565-74.
10) Joshi D, Parikh K. Synthesis and evaluation of novel benzimidazole derivatives as antimicrobial agents Medicinal Chemistry Research 2014 :1290-9.
11) Baviskar B, Baviskar B, Chuadhary S, Parwani K, Balani P, Salode V, Patil S, Khadabadi SS Synthesis of novel benzimidazole derivatives as potent antimicrobial agent RASAYAN Journal of Chemistry 2009;2(1):186-90.