



SYNTHESIS AND SIGNIFICATION OF BENZOTRIAZOLE ANALOGS IN DIFFERENT PHARMACEUTICAL DRUG.

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Article Received on 17/09/2016

Article Revised on 07/10/2016

Article Accepted on 27/10/2016

ABSTRACT

Benzotriazole being a heterocyclic compound find for their different bioactive structure. Literature indicates that compounds having Benzotriazole nucleus have wide range of therapeutic uses that include antifungal, anticonvulsant, anti-inflammatory, antidiabetic, analgesic, Anti-HIV, antitubercular, antioxidant, antidepressant, miscellaneous & antitumor activity. The purpose of this review is give an overview of different property of Benzotriazole and some of its application in synthesis of pharmacologically active drug.

KEYWORDS: Benzotriazoles, antibacterial, antifungal, heterocyclic, o-phenylenediamine.

INTRODUCTION

Benzotriazole is the six-membered heterocyclic compounds have taken a important place among various classes of organic compounds for their different effective biological activities. Among a wide variety of derivatives of Benzotriazole heterocycles that have been explored developing novel pharmaceutically important molecules. Benzotriazole compound containing three nitrogen molecule in the structure. Benzotriazole derivatives has been synthesized by the different methods. A slight change or addition of other substitution on the nitrogen molecule in the Benzotriazole nucleus can difference in their biological activities. Because of this we got the vast biological different Benzotriazole heterocycles compound properties. Benzotriazole derivatives are importantly know because for their interesting biological activity which has been seen such as antitubercular, anticancer, antioxidative, antifungal, antiviral, antibacterial, antiparasitic etc.

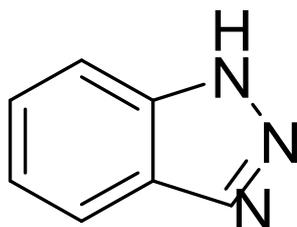


Figure.1: Skeletal formula of Benzotriazole Molecule.

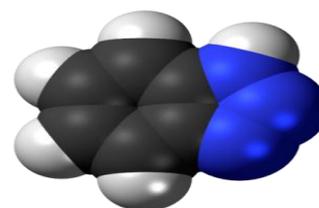


Figure.2: Spacing Model of the Benzotriazole Molecule.

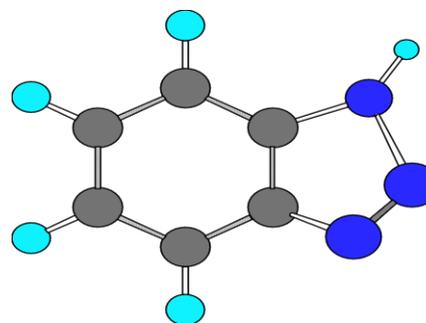


Figure.3: 3D Model of Benzotriazole Molecule.

PRODUCT SPECIFICATIONS.^[1]

Molecular Formula: C₆H₅N₃
Molecular Weight: 119.1
Appearance: White to Yellow Flakes
Assay (Min.): 99.00%
pH: 5.5 to 6.5
Melting Point: 96 to 99°
Moisture (Max.): 0.5%

Ash (Max.): 0.1%
 IR Scan: Conforms to Reference

Laboratory Synthesis of Benzotriazole

A synthesis of the Benzotriazole involves the following reaction:

The reaction among the *o*-phenylenediamine, NaNO₂ and CH₃COOH will prepare the BTA. The conversion is done by diazotization of one of the amine groups². The synthesis is able to exist better by doing it in low temperatures³ (5 to 10°C).

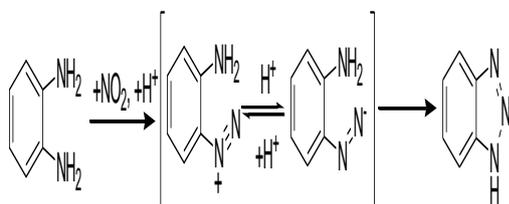


Figure.4 Synthesis of Benzotriazole ring.

Application of the Benzotriazole ring system in Drug synthesis

1. Antimicrobial Activity

Suvarna G. Kini and Co-workers^[4]

Synthesized a new series Benzotriazole derivatives (Figure.5). All the compounds were investigated for their antibacterial. They were tested on Gram positive and Gram negative bacteria. BT1 show good result against the gram positive bacteria and Gram negative bacteria.

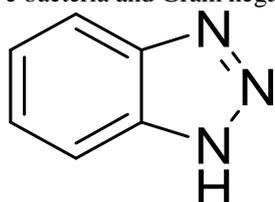


Figure.5 Benzotriazole Derivatives

S D Srivastava and Co-workers^[5]

Synthesized a new series of 2-arylidénylamino-5-(N¹-benzotriazolomethyl)-1,3,4- thiadiazoles (4) and 1-[5'-(N¹benzotriazolomethyl)-1,3,4- thiadiazol-2'-yl]-4-(substituted phenyl)-3- chloro-2-oxo-azetidines(5) derivatives (Figure.6). All the compounds were investigated for their antibacterial. They were tested on Gram positive and Gram negative bacteria. 4g,4h,4i,4j,4k,5c,5d,5e,5f,5g,5h,5i,5j and 5k show excellent result against the gram positive bacteria and Gram negative bacteria.

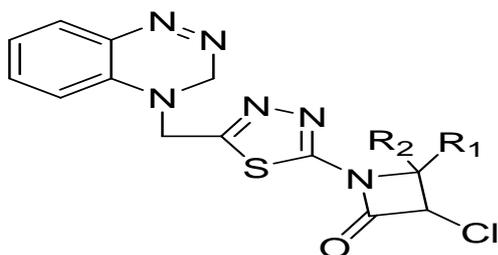


Figure.6 Benzotriazole Derivatives (4g-4k,5c-5k)

Compound	R1	R2
4g	H	C ₄ H ₃ O (furyl)
4h	H	2-OH.C ₆ H ₄
4i	CH ₃	C ₆ H ₅
4j	CH ₃	2-OH.C ₆ H ₄
4k	C ₆ H ₅	C ₆ H ₅
5c	H	-CH=CH.C ₆ H ₅
5d	H	2-Cl.C ₆ H ₄
5e	H	4-Cl.C ₆ H ₄
5f	H	4-N(CH ₃) ₂ .C ₆ H ₄
5g	H	C ₄ H ₃ O (furyl)
5h	H	2-OH.C ₆ H ₄
5i	CH ₃	C ₆ H ₅
5j	CH ₃	2-OH.C ₆ H ₄
5k	C ₆ H ₅	C ₆ H ₅

2. Antifungal Activity

Suvarna G. Kini and Co-workers^[4]

Synthesized new series Benzotriazole derivatives (Figure.7). Every the complex be study for their antifungal actions. *Candida albicans* fungi were selected for the study. Compound BT1 shows the potent activity from all the compounds.



Figure.7 Benzotriazole Derivatives

S D Srivastava and Co-workers^[5]

Synthesized a new series of 2-arylidénylamino-5-(N¹-benzotriazolomethyl)-1,3,4- thiadiazoles (4) and 1-[5'-(N¹benzotriazolomethyl)-1,3,4- thiadiazol-2'-yl]-4-(substituted phenyl)-3- chloro-2-oxo-azetidines(5) derivatives (Figure.8). All the compounds were investigated for their antifungal activities. *Candida albicans*, *Cryptosporium pannical* and *Aspergillus niger* fungi were selected for the study. Compound 4d, 4c, 4f, 4g, 4h, 4i, 4j, 4k and 5j shows the good activity from all the compounds.

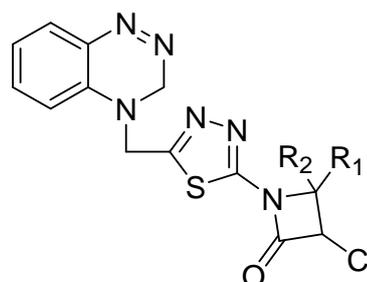


Figure.8 Benzotriazole Derivatives (4d-4k,5j)

Compound	R1	R2
4c	H	-CH=CH.C ₆ H ₄
4d	H	2-Cl.C ₆ H ₅
4f	H	4-(CH ₃) ₂ .C ₆ H ₄
4g	H	C ₄ H ₃ O (furyl)
4h	H	2-OH.C ₆ H ₄
4i	CH ₃	C ₆ H ₅
4j	CH ₃	2-OH.C ₆ H ₄
4k	C ₆ H ₅	C ₆ H ₅
5j	CH ₃	2-OH.C ₆ H ₄

3. Antioxidant Activity

C. M. Jamkhandi and Co-workers^[6]

Synthesized of benzotriazole new series of *n*-phenylacetamide and acetylcarbamic acid derivatives (Figure.9). All the synthesized compounds were investigated for antioxidant activity. The compounds A (2-(1*H*-benzotriazol-1-yl)-*N*-(4-sulfamoylphenyl)acetamide), B (2-[(1*H*-benzotriazol-1-yl)acetyl]amino] propanoic acid) and C (2-(1*H*-benzotriazol-1-yl)-*N*-(4-hydroxyphenyl)acetamide) demonstrate high-quality similar proportion of nitric oxide scavenging action. Ascorbic acid where taken as reference.

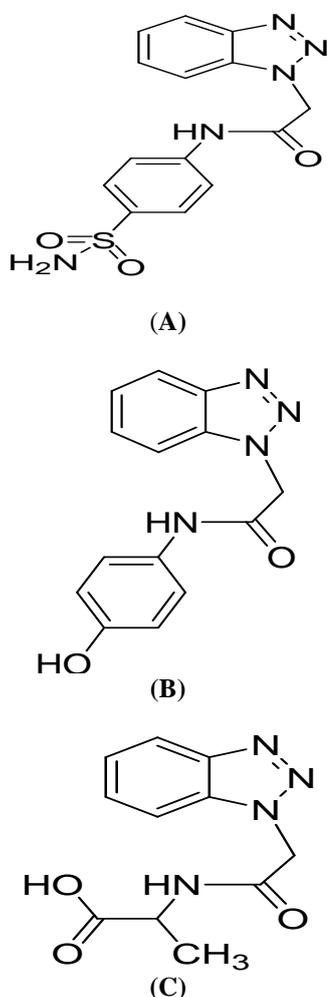


Figure. 9 Benzotriazole Derivatives

4. Anti Convulsant Activity

S D Srivastava and Co-workers^[5]

Synthesized a new series of 2-arylidénylamino-5-(*N*¹-benzotriazolomethyl)-1,3,4- thiadiazoles (4) and 1-[5'-(*N*¹benzotriazolomethyl)-1,3,4- thiadiazol-2'-yl]-4-(substituted phenyl)-3- chloro-2-oxo-azetidines(5) derivatives (Figure.10).All the compounds were investigated for their anticonvulsant activities. Pentylene tetrazole were selected as standard. Compound 4h, 5c, 5d, 5e, 5f, 5g, 5i, 5j and 5k shows the good activity from all the compounds.

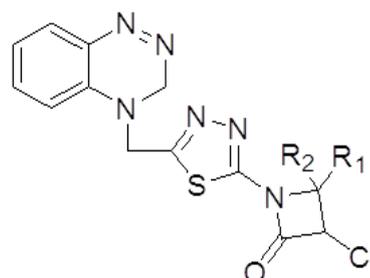


Figure.10 Benzotriazole Derivatives (4h, 5c-5k)

Compound	R1	R2
4h	H	2-OH.C ₆ H ₄
5c	H	-CH=CH.C ₆ H ₅
5d	H	2-Cl.C ₆ H ₄
5e	H	4-Cl.C ₆ H ₄
5f	H	4-N (CH ₃) ₂ .C ₆ H ₄
5g	H	C ₄ H ₃ O (furyl)
5i	CH ₃	C ₆ H ₅
5j	CH ₃	2-OH.C ₆ H ₄
5k	C ₆ H ₅	C ₆ H ₅

5. Anticancer Activity

Viswanathan CL and Co-workers^[9]

New series was synthesized of the Benzotriazole derivatives (Figure.11). The entire compound was investigated for the anticancer activity. Derivative 5 was designed and synthesized further for improve the chemo sensitizing activity of the drug. The synthesized drug shows the 29.9% inhibition of the cells growth in murine lymphocytic leukemia cell, which was best than the standard drug Verapamil which inhibit 9.3% cell growth at 80 µg/mL concentration.

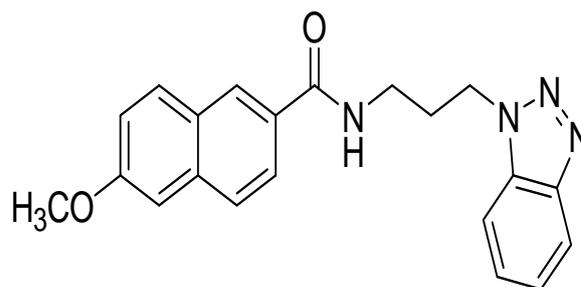


Figure.11 Benzotriazole Derivatives

Cheng CC and Co-workers^[10]

New Benzotriazole substituted aminothiazole derivative was prepared (Figure.12). The prepared derivative shows the mild activity of the anticancer.

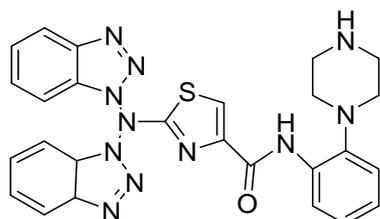


Figure.12 Benzotriazole Derivatives

Howell LA and Co-workers^[11]

New Benzotriazole containing aminoacridine derivative was synthesis (Figure.13). The prepared compound was investigated for the anticancer activity. However, when the carboxamide moiety was shift to the 3 position for the 4 position activity greatly decreased. Till today the biological target is not clear and this drug needs further more investigations.

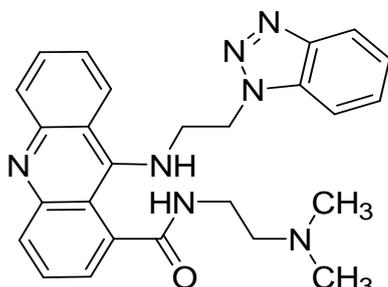


Figure.13 Benzotriazole Derivatives

6. Ant tubercular Activity**Shraddha VR and Co-workers^[12]**

Series of the amide Benzotriazole derivatives where synthesized (Figure.14). Some fragment was checked for ant tubercular activities. The compound was tested against M. Tuberculosis and comparison with the two different standard drug streptomycin and pyrazinamide.

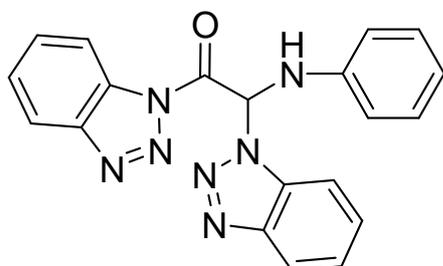


Figure.14 Benzotriazole Derivatives

Gireesh T M and Co-workers^[13]

New pyrazole containing Benzotriazole derivative was synthesized. This shows the antitubercular activity. This was seen against M. Tuberculosis and comparison with the pyrazinamide. (Figure.15)

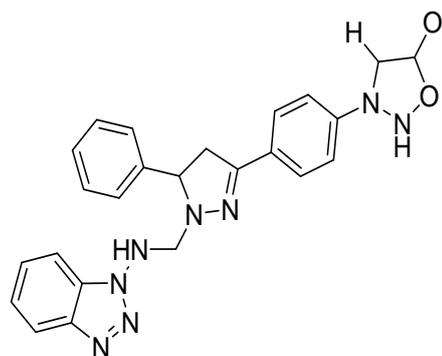


Figure.15 Benzotriazole Derivatives

7. Anti parasitic Activity**Lopez-Vallejo and Co-workers^[14]**

New Benzotriazole compounds derivative was synthesized. The synthesized derivatives was check for there ant parasitic activity. Which shoes the low micro molar activity ($IC_{50}=0.339 \mu\text{g/mL}$), which is more active than metronidazole. By changing the position of Cl group it decreased the activity. (Figure.16)

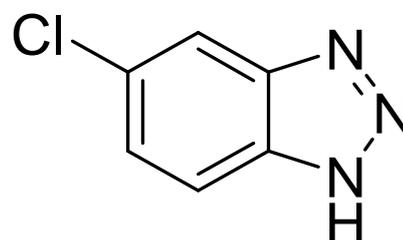


Figure.16 Benzotriazole Derivatives

8. Corrosion Inhibition**Rakesh Chandra Barik and Co-workers^[7]**

The compound Benzotriazole is added into 3.5% NaCl solution shows the corrosion inhibition on copper surface. (Figure.17)

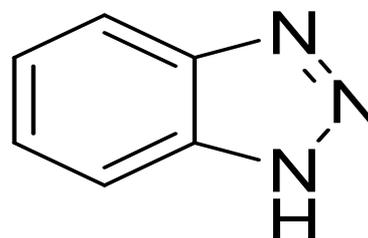


Figure.17Benzotriazole Derivatives

Ayman Ababneh and Co-workers^[8]

Synthesized a new series of Benzotriazole derivatives (Figure.18). The derivative solution shows the good corrosion inhibition activity on the surface steel. The all compound shows the good result but compound (1-Methanesulfonyl-1H-Benzotriazole) MSBTA show more good result.

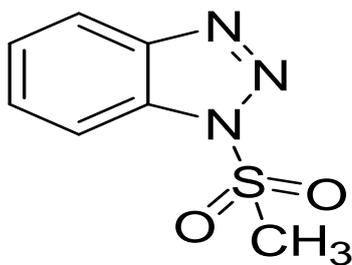


Figure.18 Benzotriazole Derivatives

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CONCLUSIONS

This review gives an overview of the broad spectrum of pharmacological activities displayed by Benzotriazole. The pharmacological activities of Benzotriazole derivatives have attracted considerable attention giving to the use full of this moiety in the field of medicinal chemistry. Further development can be carried out by making slight change leading to severe changes to yield better drug. The Benzotriazole importance of moiety can be seen by carrying out further studies on its possible substitution. Thus this paper gives to be significant for further research work on the bioactive Benzotriazole ring and biological profiles of the novel generations of Benzotriazole would represent a successful matrix for further circumstances of better medicinal agent.

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