International Journal of Medicine and Pharmaceutical Research
CODEN (USA): IJCPNH | ISSN: 2321-2624
Journal Home Page: www.pharmaresearchlibrary.com/ijmpr

REVIEW ARTICLE

An Overview on Synthesis and Biological Evaluation of Benztriazole Deravatives

Abhishek H.M, Dr. T. Yunus Pasha*

Department of Pharmaceutical Chemistry, Sri Adichunchangiri College of Pharmacy Adichunchangiri University, B.G Nagar, Mandya (D)- 571448, Karnataka, India

ABSTRACT
In the last few decades, to synthesize the different new benzotriazole compound along with their derivatives as antimicrobial activity, antifungal activity, anthelmintic activity, anti–viral activity, anti-cancer activity, anti HIV 1 activity, analgesic activity, antitubercular activity, the benzotriazole belongs to a heterocyclic compound seems to be very small compound but its activity attracted the attention of many researchers to explore this skeliton to its multiple potential against several activity. In this review we provide a brief review of benzotriazole and its derivatives has different activities.
Keywords: Benzotriazole, Antimicrobial, Antifungal, Anthelmentic, Antioxidant.

ARTICLE INFO

Corresponding Author
Dr. T. Yunus Pasha
Professor and Head
Department of Pharmaceutical Chemistry
Sri Adichunchangiri College of Pharmacy,
Adichunchangiri University, B.G Nagar,
Mandya (D)- 571448, Karnataka, India

ARTICLE HISTORY: Received 10 Feb 2020, **Accepted** 21 June 2020, **Available Online** 10 August 2020

Citation: *T. Yunus Pasha, et al.* An Overview on Synthesis and Biological Evaluation of Benztriazole Deravatives. *Int. J. Med. Pharm. Res., 2020, 8(3): 94-99.*

CONTENTS

1. Introduction

Benzotriazole is belongs to the heterocyclic compounds. Compounds which are under study since from many years. Heterocyclic compounds which are having nitrogen atom in ring are considered to be a antimicrobial agent, It can be used single or combination. know a days benzotriazole is one of the trending molecule to derive many derivative with different activity different activities of benzotriazole are antimicrobial activity[1], antifungal activity[2], anthelmentic activity [3],anti –viral activity[4-9], anti-cancer activity[5], anti HIV 1 activity[6], analgesic activity[7-10], anti tubercular activity[8]. Benzotriazole molecular formula $C_6H_5N_3$. Melting point 100^0C (212^OF; 373K) Boiling point 350^O C (662^0f; 623K). This aromatic compound is colorless and polar in nature and can be used in various field. Benzotriazole: Physical and Chemical data

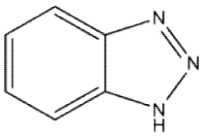
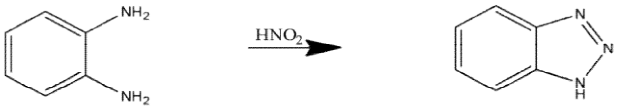


Table 1: Physical and data of Benzotriazole ring

Table number	1
Synonym:	1,2,3-Benzotriazole
CAS Number:	95-14-7
Empirical Formula (Hill Notation):	C6H5N3
Molecular Weight:	119.12
Molecular Weight:	112133
EC Number:	202-394-1
MDL number:	MFCD0005699
PubChem Substance ID:	2487810
Mp	95-99 °C
Composition	C(60.50%) H(4.23%) N(35.27%)
Molar Refractivity	34.71 ± 0.3 cm3
Molar Volume	88.3 ± 3.0 cm3

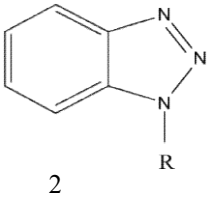
2. Synthesis of benzotriazole

Benzotriazole is prepared by treating o-phenylenediamine with nitrous acid (liberated during the reaction between sodium nitrite and acetic acid) to form mono-diazonium salt that follows spontaneous intramolecular cyclization reaction to produce benzotriazole.



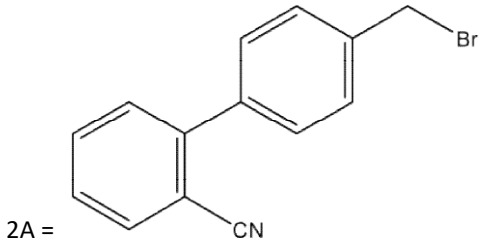
O- phenylenediamine Benztriazole

S. Nanjunda Swamy, *et al.*,[11] synthesized a new antimicrobial agent. He was synthesized benztrizole derivatives and evaluated their efficacy as antimicrobials by disc diffusion method against different strains. 2a,2c,2e,2g str 1.

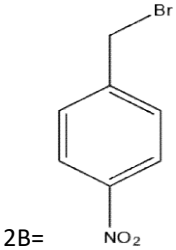


2

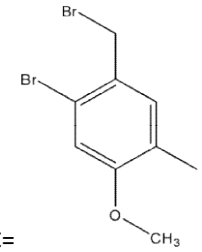
Were R-X=2A,2B,2C,2D,2E,2F and 2G



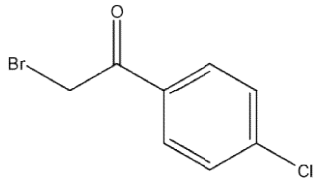
2A =



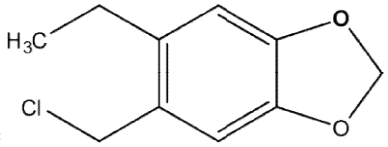
2B=



2C=



2D=

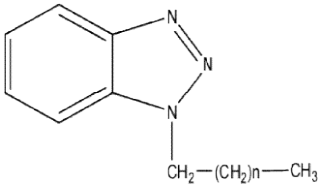


2E=

2F=CH_3-CH_2-CH_2-Br

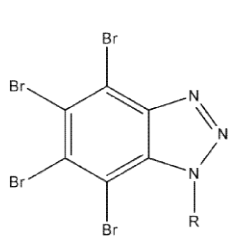
2g=CH_3-CH_2-CH_2-CH_2-Br

2) Zahra Rezaei *et al*.,[12] carried docking studies of azoles compounds plus fluconazole in the active site of cytochrome P450 14a-sterol demethylase. Triazole derivatives showed more negative docking energy in the comparison with benzotriazole derivatives. The synthesed compound 2 shows better activity.

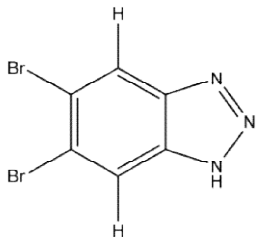


n=3 2

3) katarzyna kopanska., *et al.,* [13] Design and synthesis of Bromo- chloro and methyl-analogues of benzotriazole and their derivatives and screened them for in vitro antiprotozoal activity in that 3and 4 compound showed higher efficacy against the acantamoeba cysta.

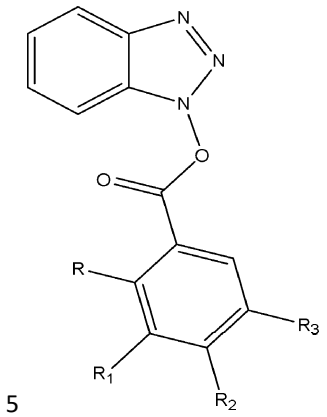


3



4

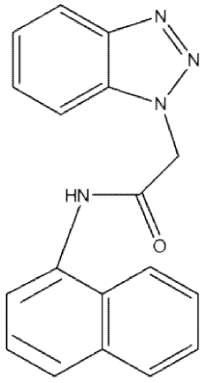
4) Dabhade P.S *et al*.,[14] in order to designe, synthesis and evaluation of antifungal activity of benztriazole invitro activity has done for the synthesized compound by using tube dilution method and reported that B11, B13, B16, B18 compound showed potent activity against T.rubrum.



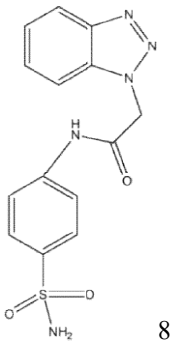
5

SL NO	R1	R2	R3
B11	CL	H	H
B13	CL	H	NO_2
B16	CL	H	NO_2
B18	CL	CH_2	H

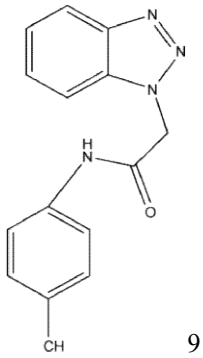
5) C. M. Jamkhandi *et al. ,* [15] Design and synthesis of Benzotriazole derivatives 7,8 and 9 showed powerful comparable percentage of nitric oxide scavenging activity with the standards reference ascorbic acid and other derivatives showed medium antioxidant activity.



7

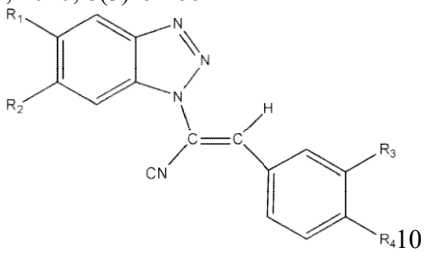


8



9

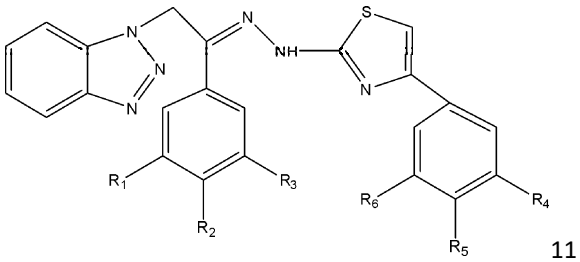
6) Antonio Carta *et al.,* [16] Design and synthesis of benzotriazole derivatives as anti proliferative agent. The new 3-aryl-2-acrylonitriles, and 3-aryl-2-acrylonitriles, reported and tested for cytotoxicity against MT-4 cells and for anti-tubercular activity against some of strains of M. tuberculosis. The cytotoxicity against MT-4 cells is reported. The compounds like 10a, 10b, 10c (g,I,j). showed a better anti proliferative activity.



10

SL NO	R1	R2	R3	R4
G	CH_3	CH_3	NO_2	H
I	CF_3	H	NO_2	H
J	H	CF_3	NO_2	H

7) Nitin D *et al*., [17] synthesis and biological evaluation of novel thiazole substituted benzotriazole derivatives as antimicrobial agents. A series of novel hybrid molecules containing thiazole and benzotriazole templates were designed & synthesized. All the synthesized compounds were evaluated for their antimicrobial activity against Gram-positive, Gram-negative strains of bacteria and fungal strains. After that minimum inhibitory concentrations, minimum bactericidal concentrations and minimum fungicidal concentrations of all the synthesized compounds were determined. The compounds like 11a, 11b, 11c showed a better anti microbial activity.

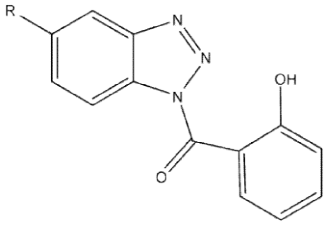


11

SL NO	R1	R2	R3	R4	R5	R6
11A	H	F	H	H	F	H
11B	H	F	H	H	CL	H
11C	H	F	H	H	Br	H

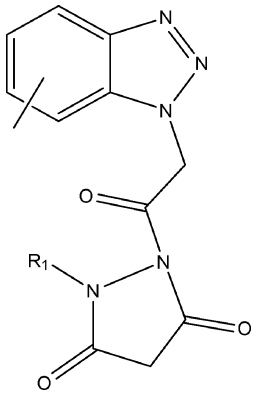
8) Giuliana Biagi *et al*., [18] has reported the synthesis and pharmacological evaluation of a series of 1,2,3-triazolyl-benzimidazolone and 1,2,3-triazolyl-benzotriazole derivatives. These compounds had been studied for their structural relationships with the benzimidazolone derivatives. However, the triazolylbenzotriazole derivatives showed better vasodilator activity & potency than the corresponding benzimidazolone derivatives.

SL NO	R
A	H
B	CH_3
C	CL
D	F
E	CF_3
F	C_6H_5



12B

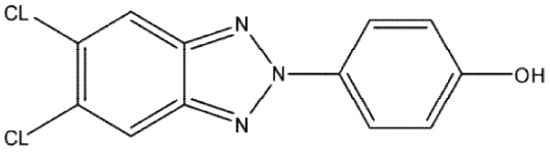
9) B.V Suma *et al.,* [19] synthesis and designe of benztriazole derivatives as antibacterial activity. Compound 13H is more effective to against S. aureus, compound 13F is more effective against B.subtilis. Compound 13B is more activity against E.coli. Compound 13G is more activity against P. vulgaris. Accordingly, in Antifungal activity, Compounds 13E and 13H and 13I were found to be good activity against A.niger while compounds 13C and 13G were found to have good activity against C. albicans.



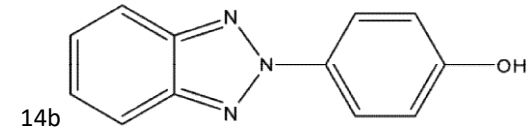
13

Compound	R	R1
13A	H	H
13B	H	C_6H_5
13C	H	$C_6H_5N_2O_2$
13D	H	C_6H_6CL
13E	CL	H
13F	CL	C_6H_5
13G	CL	$C_6H_4N_2O_2$
13H	CL	C_6H_5CL
13I	NO_2	H

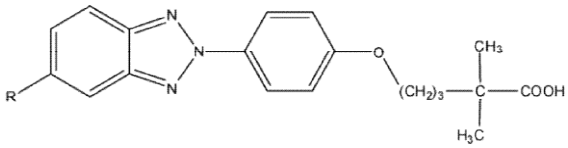
10) Roberta Loddo et al., [20] designe and synthesis of benztriazole as antiviral activity. in 64 deivatives 17 of them, [4-(benzotriazol-2-yl) phenoxy] alkanoic acids)] were screened for antiviral activity against the panel of twelve DNA & RNA viruses. CVB-5, RSV, BVDV, Sb-1 and YFV were, in decreasing order, the more effectively affected viruses; DENV-2, WNV, HIV-1 and Reo-1 were only occasionally and modestly affected, while the other remaining viruses were not affected by any of tested compounds. Worth of note were the compounds14a and 14b; the former for the activity against Sb-1 (EC50 = 7 lM). In particular, compound 14c displayed a potent and selective activity against CVB-5 with EC50 = 0.15 lM and SI = 100, thus representing a valuable hit compound for the development of antiviral agents for the treatment of human pathologies related to this virus.



14a

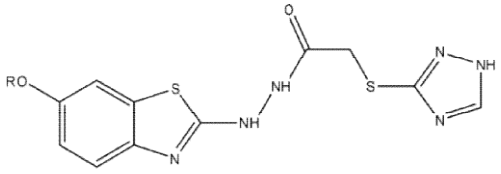


14b



14c

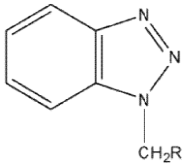
11) Da-Chuan Liu etal.,[21] synthesis and design of benzotriazole as anticonvulsant agent. Reported that 15i and 15j showed more potent activity as anticonvulsant activity.

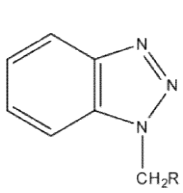


15

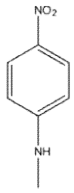
COMPOUND	R
15I	CH2C6H4
15J	CH2C6H4

12) S. S. Pawar et al.,[22]reported that design synthesis of benztriazole derivatives has anthelmintic property. reported N1 alkyl/Arylaminomethylene benzotriazoles and the N1 alkoxy/Aryloxymethylene Benzotriazoles showed the significant anthelmintic activity at the dose 5, 10 and 15 mg/ml in that N1 – (p-nitrophenyl) aminomethylenebenzotriazole and the N1 – benzyloxymethylenebenzotriazole showed the best potent anthelmintic activity. 15a and 15d shows faster activity



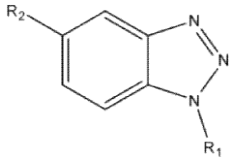


R=

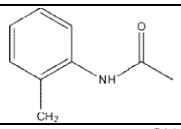
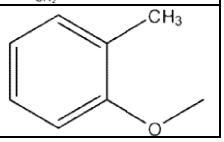


R=

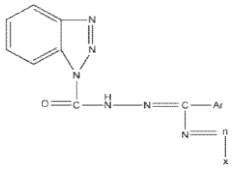
13) Jay J. Shah et al.,[23] design and synthesis of benztriazole derivatives as novel antifungal agent. Reported inhibition of ergosterol biosynthesis 8a & 9a showed greater antifungal activity against C. albicans 16A and 16B showed greater activity.



16

COMPOUND	R1	R2
16A	H	
16B	H	

14) M.S. Sudhir et al.,[24] designe and synthesis of benzotriazole derivatives as anthelmintic agents. the compound (…….) showed higher activity when Ar =$C_6H_4NO_2$



17

Source of Funding
No source of funding

Conflict of Interest
No interest

3. Acknowledgement
I am very thankful to Dr. T yunus pasha sir HOD of Pharma chemistry and Principle of Adichunchangiri college of Pharmacy, Adichunchungiri University, B.G Nagar, Mandya, Karnataka to providing me all the facilities to carry out of my work and my M pharma cource.

4. Reference
[1] Suma BV, Natesh NN, Venkataramana CH, Jays J, Madhavan V. Synthesis and antibacterial of some new 1, 2, 3 benzotriazoles derivatives containing pyrazolidinedione moieties. Int J Pharm Pharm Sci. 2012;4(1).

[2] Khabnadideh S, Rezaei Z, Pakshir K, Zomorodian K, Ghafari N. Synthesis and antifungal activity of benzimidazole, benzotriazole and aminothiazole derivatives. Research in pharmaceutical sciences. 2012 Apr;7(2):65.

[3] Sudhir MS, Nadh RV. Evaluation of in vitro anthelmintic activities of novel 1, 2, 3–benzotriazole derivatives synthesized in ultrasonic and solvent free conditions. Journal of Pharmacy Research. 2013 Jan 1;7(1):47-52.

[4] Asif M. Antiviral and antiparasitic activities of various substituted triazole derivatives: A mini. Chem Int. 2015;1(2):71-80.

[5] Ren Y, Zhang L, Zhou CH, Geng RX. Recent development of benzotriazole-based medicinal drugs. Med. chem. 2014;4(9):640-62.

[6] Asif M. Antiviral and antiparasitic activities of various substituted triazole derivatives: A mini. Chem Int. 2015;1(2):71-80

[7] Caliendo G, Di Carlo R, Greco G, Meli R, Novellino E, Perissutti E, Santagada V. Synthesis and biological activity of benzotriazole derivatives structurally related to trazodone. European journal of medicinal chemistry. 1995 Jan 1;30(1):77-84.

[8] Sanna P, Carta A, Nikookar ME. Synthesis and antitubercular activity of 3-aryl substituted-2-(1H (2H) benzotriazol-1 (2)-yl) acrylonitriles. European journal of medicinal chemistry. 2000 May 1;35(5):535-43.

[9] Loddo R, Novelli F, Sparatore A, Tasso B, Tonelli M, Boido V, Sparatore F, Collu G, Delogu I, Giliberti G, La Colla P. Antiviral activity of benzotriazole derivatives. 5-[4-(Benzotriazol-2-yl) phenoxy]-2, 2-dimethylpentanoic acids potently and selectively inhibit Coxsackie Virus B5. Bioorganic & medicinal chemistry. 2015 Nov 1;23(21):7024-34.

[10] Sondhi SM, Dinodia M, Kumar A. Synthesis, anti-inflammatory and analgesic activity evaluation of some amidine and hydrazone derivatives. Bioorganic & medicinal chemistry. 2006 Jul 1;14(13):4657-63.

[11] Swamy SN, Sarala G, Priya BS, Gaonkar SL, Prasad JS, Rangappa KS. Microwave-assisted synthesis of N-alkylated benzotriazole derivatives: Antimicrobial studies. Bioorganic & medicinal chemistry letters. 2006 Feb 15;16(4):999-1004.

[12] Rezaei Z, Khabnadideh S, Pakshir K, Hossaini Z, Amiri F, Assadpour E. Design, synthesis, and antifungal activity of triazole and benzotriazole derivatives. European journal of medicinal chemistry. 2009 Jul 1;44(7):3064-7.

[13] Kopańska, K., Najda, A., Żebrowska, J., Chomicz, L., Piekarczyk, J., Myjak, P. and Bretner, M., 2004. Synthesis and activity of 1H-benzimidazole and 1H-benzotriazole derivatives as inhibitors of Acanthamoeba castellanii. *Bioorganic & medicinal chemistry*, *12*(10), pp.2617-2624.

[14] Dabhade PS. Synthesis and evaluation of antifungal activity of benzotriazole derivatives. Asian Journal of Biomedical and Pharmaceutical Sciences. 2013 Feb 1;3(17):29.

[15] Jamkhandi CM, Disouza JI. Evaluation of antioxidant activity for some benzotriazole substituted with N-phenylacetamide and acetylcarbamic acid derivatives. International Journal of Pharmacy and Pharmaceutical Sciences. 2013, 5(2): 249-53.

[16] Carta A, Palomba M, Boatto G, Busonera B, Murreddu M, Loddo R. Synthesis and antiproliferative activity of 3-aryl-2-[1H (2H)-benzotriazol-1 (2)-yl] acrylonitriles variously

substituted: Part 4. Il Farmaco. 2004 Aug 1;59(8):637-44.

[17] Gaikwad ND, Patil SV, Bobade VD. Synthesis and biological evaluation of some novel thiazole substituted benzotriazole derivatives. Bioorganic & medicinal chemistry letters. 2012, 22(10):3449-54.

[18] Biagi G, Giorgi I, Livi O, Scartoni V, Barili PL, Calderone V, Martinotti E. New 5-substituted-1-(2-hydroxybenzoyl)-benzotriazoles, potassium channel activators. IV. Il Farmaco. 2001 Nov 1;56(11):827-34.

[19] Suma BV, Natesh NN, Venkataramana CH, Jays J, Madhavan V. Synthesis and antibacterial of some new 1, 2, 3 benzotriazoles derivatives containing pyrazolidinedione moieties. Int J Pharm Pharm Sci. 2012;4(1). Suma BV, Natesh NN, Venkataramana CH, Jays J, Madhavan V. Synthesis and antibacterial of some new 1, 2, 3 benzotriazoles derivatives containing pyrazolidinedione moieties. Int J Pharm Pharm Sci. 2012;4(1).

[20] Loddo R, Novelli F, Sparatore A, Tasso B, Tonelli M, Boido V, Sparatore F, Collu G, Delogu I, Giliberti G, La Colla P. Antiviral activity of benzotriazole derivatives. 5-[4-(Benzotriazol-2-yl) phenoxy]-2, 2-dimethylpentanoic acids potently and selectively inhibit Coxsackie Virus B5. Bioorganic & medicinal chemistry. 2015 Nov 1; 23(21):7024-34.

[21] Liu DC, Zhang HJ, Jin CM, Quan ZS. Synthesis and biological evaluation of novel benzothiazole derivatives as potential anticonvulsant agents. Molecules. 2016 Mar;21(3):164.

[22] Pawar SS, Gorde PL, Kakde RB. Synthesis of new N1-substituted benzotriazoles as anthelmintic agents. Arch Appl Sci Res. 2010;2(1):80e85.

[23] Shah JJ, Khedkar V, Coutinho EC, Mohanraj K. Design, synthesis and evaluation of benzotriazole derivatives as novel antifungal agents. Bioorganic & medicinal chemistry letters. 2015 Sep 1;25(17):3730-7.

[24] Sudhir MS, Nadh RV, Radhika S. Antifungal activities of novel 1, 2, 3-benzotriazole derivatives synthesized by ultrasonic and solvent-free conditions. Drug invention today. 2013 Jun 1;5(2):126-32.