International Journal of Pharmaceutical Chemistry
ISSN: 2249-734X (Online)
CODEN: IJPCH3 (American Chemical Society)
Journal DOI: https://doi.org/10.7439/ijpc **Review Article**

Benzotriazole, its derivatives and antibacterial activity: An overview

A. S. Gujar*, K. R. Danao and U. N. Mahajan

Department of pharmaceutical chemistry, Dadasaheb Balpande College of Pharmacy, Besa, Nagpur, Maharashtra, India

Abstract

Benzotriazole is an important class of bicyclic heterocyclic compounds were consist of three N atoms in cyclopentene and fused benzene ring. Its molecular formula is $C_6H_5N_3$. It is rarely obtained in natural but their synthesis is easy to perform. On screening the literature, benzotriazole gave a comprehensive review of the latest and remarkable developments of benzotriazole derivatives covering a varied number of activities such as antifungal, antibacterial, anticancer, anthelmintic, antidepressant, antioxidative, antitubercular, antiviral, anti-inflammatory, etc. The present reviews attempted to assemble the various derivatives of benzotriazole and its antibacterial activities.

Keywords: Benzotriazole, Benzotriazole derivatives, Antibacterial activities.

***Correspondence Info:**
A. S. Gujar,
Department of pharmaceutical chemistry,
Dadasaheb Balpande College of Pharmacy,
Besa, Nagpur, Maharashtra, India

***Article History:**
Received: 14/03/2020
Revised: 25/03/2020
Accepted: 29/03/2020
DOI: https://doi.org/10.7439/ijpc.v10i3.5474

QR Code

How to cite: Gujar A. S, Danao K. R. and Mahajan U. N. Benzotriazole, its derivatives and antibacterial activity: An overview. *International Journal of Pharmaceutical Chemistry* 2020; 10(3): e5474. Doi: 10.7439/ijpc.v10i3.5474 Available from: https://ssjournals.com/index.php/ijpc/article/view/5474

1. Introduction

Benzotriazole is an important class of bicyclic heterocyclic compounds, were consist of three N atoms with fused benzene ring [1]. Its five-membered rings can show tautomerism. Its common structure is stated in figure 1[2]. It is important in the dairy industry due to its ability to inhibit metal corrosion [3]. Benzotriazole is inexpensive and stable. It is acidic (pKa 8.2) and is easily soluble in alkaline solutions. It is a soluble organic solvent like ethanol, benzene, toluene, chloroform, and DMF [4]. The fused benzene ring makes benzotriazole nucleus possess a larger conjugated system to form π-π stacking interactions, [In chemistry, *pi* stacking (also called **π–π** stacking) refers to attractive, noncovalent interactions between aromatic rings, since they contain *pi* bonds], and its three nitrogen atoms make it easy to form hydrogen bonds and coordination bonds, thereby benzotriazole derivatives are more ready to bind with a variety of enzymes and receptors in the biological system via diverse non-covalent interactions, resulting in a broad spectrum of biological activities[5]. Benzotriazole possesses both electrons–donor and electron–acceptor properties. Benzotriazole has been investigated for a broad spectrum of activities which include antibacterial, antiviral, anti-inflammatory, anticonvulsant, an enzyme inhibitor, DNA cleavage, antifungal, herbicidal, antitubercular, antimicrobial and antiproliferative[6]. As the microorganisms are rapidly undergoing genetic changes and developing resistance against the many antibiotics and therapeutic agents for various diseases more quickly than the new drugs are being made available to the war against the infectious diseases has become a never-ending process[7]. Benzotriazole showed a wide application in pharmaceutical purposes to treat diseases [8]. Especially, triazole derivatives as medicinal drugs have been playing important roles in medicinal chemistry [9], and a lot of triazole analogs including imidazole, thiazole, carbazole, oxazole and benzimidazole [10], etc. have also been found to be widely

used in the clinic. It is a fused aromatic nitrogen-containing heterocyclic compound and its derivatives have the various biological and industrial applications [11], corrosion inhibitors [12], man-made materials [13], supramolecular ligands [14], therefore large numbers of researches have already been focused on this attractive area. Moreover, a variety of benzotriazoles have been reported to inhibit the growth of some microorganisms and some benzotriazole derivatives show anti-inflammatory properties [15]. Benzotriazole is inexpensive and stable compound [16]

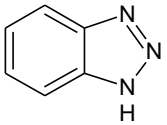


Fig. 1H-Benzotriazole

1.1 Physiochemical properties

Table 1: Physicochemical properties of Benzotriazole

Common name	Benzotriazole
IUPAC name	1-H Benzotriazole, 1,2,3 Benzotriazole
Molecular formula	$C_6H_5N_3$
Molecular weight	119.12g mol^{-1}
Appearance	Solid
Colour	White to tan crystalline powder
Odour	Odourless
Density	1.36gcm^{-3}
Melting point	100^{0}C
Boiling point	350^{0}C
Solubility	Soluble in water (20g/lit)

1.2 Mechanics of benzotriazole[17]

Benzotriazole

⇩

Ability to permit /enter into

⇩

Membrane of microbes

⇩

Damages the membrane of the microbes cell membrane

⇩

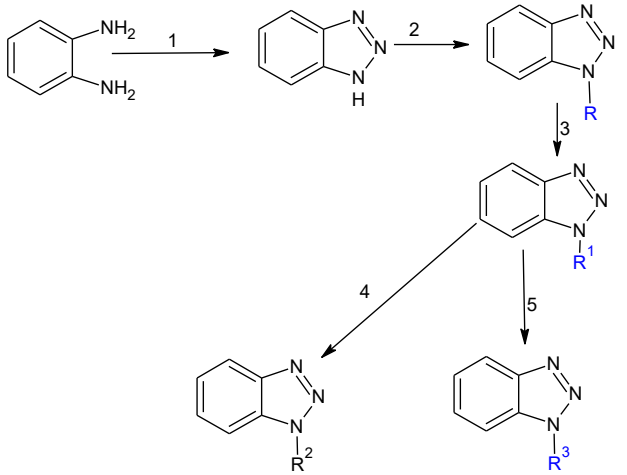
Leakage out the content

⇩

Death of microbes

1.3 Scheme of synthesis benzotriazole dervivatives[18]

Figure 2: Mechanics of the benzotriazole derivative

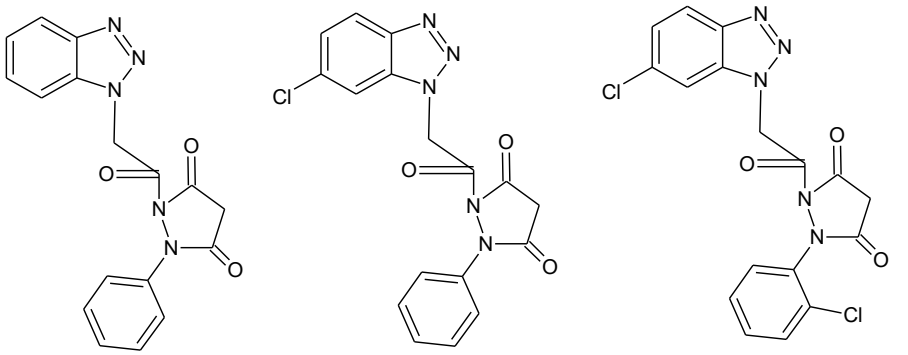


R	CH2COOC2H5
R^1	CH2CONH-NH2
R^2	CH2CONH-N=CH-D
R^3	CH2CONH-N=C-D

1 = Sodium nitrite, Glacial Acetic acid, water.
2 = Ethyl chloroacetate, Dry acetone.
3 = Hydrazine hydrate, methanol.
4 = Methanol, Aromatic aldehydes.
5 = Methanol, Aromatic ketones.
D = N, N Dimethyl amino benzaldehyde, 4-OH Benzaldehyde

2. Antibacterial activity

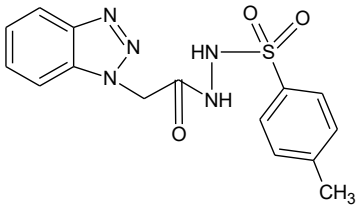
A series of 1, 2, 3, benzotriazole derivatives containing pyrazolidine 3, 5 dione moiety were synthesized by diazotization of benzene-1, 2-diamine with glacial acetic acid and were evaluated for antibacterial activities, against gram-positive organisms like *S. aureus* and *B. subtilis* as well as gram-negative organisms like *E. Coli* and *P. vulgaris* by diffusion agar media technique. Compound 1b (Fig. 1) was found to be good activity against *E. coli.* Compound 1h (Fig. 1) was found to be more effective against *S. aureus*. Compound 1f was found to have good activity against *B. subtilis*. Compound 1g (Fig. 1) was found to have good activity against *P. Vulgaris.* Ciprofloxacin and Amoxicillin (100 µg/ml) was used as a standard for screening [19].



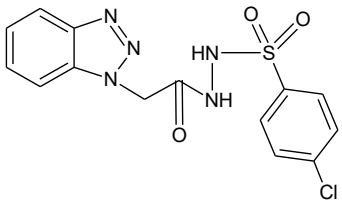
Compound 1 a Compound 1 b Compound 1 c

Fig. 2: Compound 1 h, 1 b, and 1 g

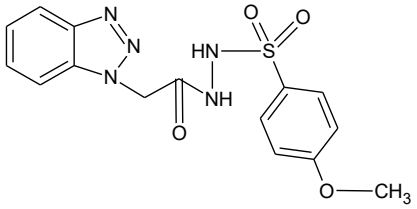
N-Substituted 2- (1H-benzotriazole – 1 - yl) - acetohydrazide series (2a-2f) were synthesized from o-phenylenediamine and evaluated for antibacterial activity by agar plate disc diffusion method. Compound 2b, 2c, and 2e (Fig. 2) showed good antibacterial activity against *S. aureus*, *B. subtilis,* and *E. coli* but less potent than sulphacetamide[20].



Compound 2 d



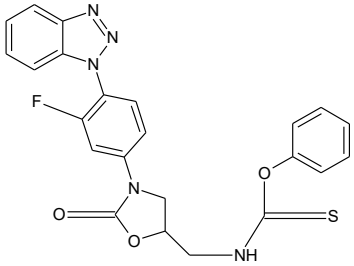
Compound 2 e



Compound 2 f

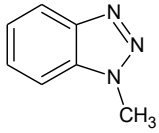
Fig. 3: Compound 2 d, 2 e, and 2 f

Sanna *et al* was synthesized a series of acrylonitrile containing benzotriazole derivatives and exhibited antitubercular activity against many antibiotic-resistant microbial strains. Compound 3 (Fig. 3) showed excellent antibacterial activity against antibiotic-resistant microbial strains [21].



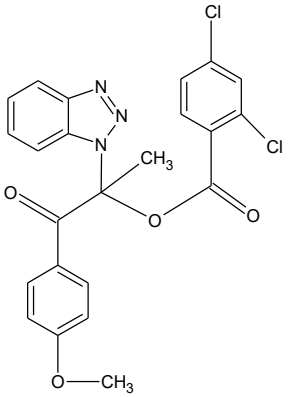
Compound 3 a

A series of N-alkylated benzotriazole derivatives were synthesized and evaluated for antimicrobial activity. Compound 4 (Fig. 4) showed significant antimicrobial activity against many gram-positive and gram-negative bacteria [22].



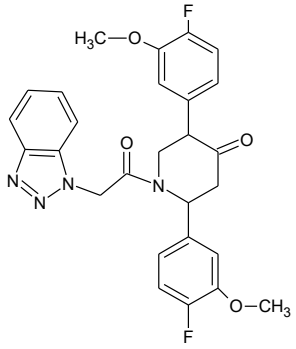
Compound 4 a

A novel series of N-Substituted benzotriazole derivatives containing mannich bases (5a-5x) were synthesized by amine exchange reactions, from the N, N-dimethylaminopropiophenone hydrochlorides and benzotriazole. Antibacterial activities of the synthesized compounds were tested against *B. subtilis*, *S. aureus*, *S. faecalis, E. coli, P. aeruginosa,* and *E. cloacae* using MHA media. Compounds 5d (Fig. 5), 5g, 5p 5r, and 5x exhibited significant activity with MIC values of 1·56 µg/mL against *B. subtilis*. Compound 5s (Fig. 5) showed the most favourable antibacterial activity against *B. subtilis, S. aureus, S. faecalis, P. aeruginosa, E. coli* and *E. Cloacae* with MIC of 1·562 µg/mL, 1·562 µg/mL, 1·562µg/mL, 3·125 µg/ mL, 6·25 µg/mL and 6·25µg/mL respectively[23].



Compound 5 a

A series of imidazole/benzotriazole substituted piperidine-4-one derivatives (6a–6j) were synthesized. The synthesized compounds were investigated for antimicrobial activity against selected bacterial strains. Among the compounds, fluoro and methoxy group substituted compound 6d (Fig. 6) showed good antimicrobial activity at minimum concentration [24].



Compound 6d

Benzotriazole derivatives

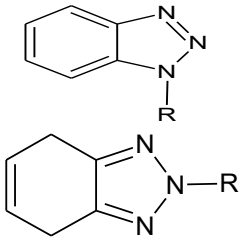


Table 2: Antibacterial activity of Benzotriazole derivatives

Year	Benzotriazole derivative (R- Substitute)	Author/Investigator's	Reported activity	Reference No.
1992	Chloro substituted phenoxy acetyl and propionyl benzotriazoles	M Purohit and SK Srivastava	Antibacterial, Antifungal	[25]
1994	Derivatives of 1-(Nheteroyl/diphenyl amino acetyl/propionyl) benzotriazole	Upadhaya RK and Srivastav SD	Antibacterial, Antifungal, Anthelmintic	[26]
1994	Benzotriazolesulfinic acid derivatives	Peter Ackerman and Max Schellenbaum	Antifungal	[27]
2000	Derivatives of pyrazol-2(1H(2H) benzotriazol	Taha M.A	Antimycobacterial activity	[28]
2002	Benzotriazole derivatives of 2aminothiophene-3-carbonitrile, 2thioxopyridine-3-carbonitrile, 1,8naphthyridine-2-one, thieno[2,3b]pyridine-5-carbonitrile and thieno[2,3-d]pyrimidine	Fatima A.O.	Antibacterial, antifungal	[29]
2003	Dialkylamino side-chain substituted on the Benzotriazole	Kuo-Long Yu	Respiratory syncytial virus	[30]
2004	5,6-dimethyl-1H benzotriazole and 5,6-dibromo-1H-benzotriazole	Katarzyna K	inhibitor of Acanthamoebacastellanii	[31]
2005	Oxazolidinone derivatives with positional and geometrical substitutions on benzotriazole	Jagattaran Das	Antibacterial activity	[32]
2005	Benzotriazolyloxazolidinone derivatives	Prasad PD and co-workers	Antibacterial activity	[33]
2005	N-alkyl derivatives of 1Hbenzotriazole	Maria B.	Antihelicase activity against Flaviviridae	[34]
2006	5-arylidene-2-aryl-3(benzotriazoloacetamidyl)-1,3thiazolidin-4-ones	KC Asati	Antibacterial activity	[35]
2006	Derivatives of N-alkylated benzotriazole	S Nanjund Swamy	Antibacterial activity, Antifungal	[36]
2006	Benzotriazole esters	Chung-Yi Wu	SARS activity	[37]
2006	Derivatves of 1-[3-(4-benzotriazol1/2-yl-3-fluoro-phenyl)-2-oxooxazolidin-5-ylmethyl]-3substituted-thiourea	Prasad PD and coworkers	Antitubercular activity	[38]
2008	Derivatives of 5-[2-(1,2,3benztriazole)-1-yl-methyl]-1′arylidene hydrazine-1,3,4thiadiazoles and 5-[2-(1,2,3benztriazole)-1-yl-methyl]-1′-(4′substituted aryl-3′-chloro-2′-oxo azetidine)]-amino-1,3,4-thiadiazoles	Shukla DK and Srivastav SD	Antibacterial activity, Antifungal	[39]
2008	Derivatives of Benzotriazole esters1-(4Dimethylaminobenzoyloxy)- Benzotriazole	Koen HG	SARS activity	[40]

2009	2-(substituted)-5-[(NBenztriazolomethyl)-1,3,4Thiadiazolyl]-4 Thiazolidinones	KP Namdeo	Antifungal	[41]
2009	Derivatives of 1-Trityl-1H-1,2,3-	Rezaei Z	Antifungal	[42]
2010	1H-Benzotriazolylpropanone and 2H-benzotriazolylpropanones	Jun Wan and coworkers	Antibacterial activity	[43]
2010	Acridine substituted Benzotriazole derivative	Singh NP	Antibacterial activity	[44]
2010	Derivatives of 2-(2,4difluorophenyl)-1-(2,3-dihydro-1Hbenzotriazol-1-yl)-3-(1H-1,2,4triazol-1-yl)propan-2-ol	Pallav D. Patel	Antifungal	[45]
2011	Imidazole/benzotriazole substituted piperidine-4-one derivatives	Ramachandran R.	Antibacterial activity, Antifungal	[46]
2011	Azetidinone derivatives of benzotriazole.	Dubey A and coworkers	Antitubercular activity	[47]
2011	Triazoloquinolones	Carta Antonio	Antitubercular activity	[48]
2012	Benzotriazole derivatives substituted with thiazole moiety.	Gaikwad ND and coworkers	Antibacterial activity, Antifungal	[49]
2012	Nonyl, Decyl, Dodecyl substituted Benzotriazole derivatives	S. Khabnadideh and coworkers	Antifungal	[50]
2012	N-Substituted 2-(1H-benzotriazole-1yl) -acetohydrazide derivatives	Jimit S. Patel	Antibacterial activity, Antifungal	[51]
2012	Benzotriazole substituted with pyrozolidine 3, 5-dione.	BV Suma	Antibacterial activity	[52]
2013	1,2,3-benzotriazole derivatives synthesized by ultrasonic and solvent-free conditions	MS Sudhir	Antifungal activities	[53]
2014	Benzotriazolo-thiadiazolyl-imidazole derivative	VK Singh	Anticonvulsant, Antimicrobial activity	[54]
2015	1H-benzotriazol-1-yl(2-hydroxy -5- [(e) phenyldiazenyl] phenyl) methanone derivatives	CM Jamkhandi	Anti-inflammatory activity	[55]
2017	2-(2-hydroxyaryl) benzotriazoles	Farkas R	Antibacterial, Antifungal, Antiviral, Anthelmintic, Antiprotozoal, And Antimycobacterial Activity	[56]

3. Research in Context

1) **Systematic review:** Benzotriazole derivative has chemical and biological properties that are versatile in the pharmaceutical industry. Benzotriazole derivatives act as agonists for many proteins.
2) **Interpretation:** Our data show that the 245 derivative of benzotriazole is available & it is arranged in the year wise in the form of graphical representation.
3) **Future directions:** Benzotriazole provide the information of antibacterial activity still it has required research for futuristic pharmacological action.

4. Conclusion

The literature study of investigations on the synthesis and antimicrobial screening of Benzotriazole derivatives in the past two decades showed antimicrobial activities like antibacterial, antifungal, antiviral, antiprotozoal, and anthelmintic action. From the above, we conclude that the benzotriazole derivative shows the strongly potent antibacterial activity against the gram-positive and gram-negative bacteria.

References

[1]. Peng XM, Cai GX, Zhou CH. Recent developments in azole compounds as Antibacterial and antifungal agents. *Curr Top Med Chem* 2013; 13: 1963-2010.

[2]. Zhou CH, Wang Y. Recent researches in triazole compounds as medicinal drugs. *S Curr Med Chem* 2012; 19: 239-280.

[3]. Wei JJ, Wang Y, Wang XL, Zhou CH, Ji QG. Recent developments of 2,3-triazoles in medicinal chemistry. *Chin Pharm J* 2011; 46: 481-485.

[4]. Pasqualotto AC, Thiele KO, Goldani LZ. Novel triazole antifungal drugs: focus on isavuconazole, ravuconazole and albaconazole. *Curr Opin Investig Drugs* 2010; 11: 165-174.

[5]. Zhang L, Peng XM, Damu GL, Geng RX, Zhou CH. Comprehensive review in current developments of imidazole-based medicinal chemistry. *Med Res Rev* 2014; 34: 340-437.

[6]. Cui SF, Wang Y, Lv JS, Damu GLV, Zhou CH. Recent advances in application researches of thiazole compounds. *Scientia Sinica Chimica* 2012; 42: 1105-1131.

[7]. Zhang FF, Gan LL, Zhou CH. Synthesis, antibacterial and antifungal activities of some carbazole derivatives. *Bioorg Med Chem Lett* 2010; 20: 1881-1884.

[8]. Zhou CH, Zhang FF (2011) Process for preparation of carbazole containing chalcone derivatives. CN Patent CN101993432 (A).

[9]. Zhang HZ, Zhou CH, Geng RX, Qing-Gang JI. Recent advances in syntheses of oxazole compounds. *Chin. J Org Chem* 2011; 31: 1963-1976.

[10]. Zhang SL, Damu GL, Zhang L, Geng RX, Zhou CH. Synthesis and biological evaluation of novel benzimidazole derivatives and their binding behavior with bovine serum albumin. *Eur J Med Chem* 2012; 55: 164-175.

[11]. Abbas Al-Mulla,A Review: Biological Importance of Heterocyclic Compounds. *Der Pharma Chemica*, 2017; 9(13): 141-1472.

[12]. Liu YS, Ying GG, Shareef A, Kookana RS. Biodegradation of three selected benzotriazoles in aquifer materials under aerobic and anaerobic conditions. *J Contam Hydrol* 2013; 151: 131-139.

[13]. Wang L, Zhao L, Xue RY, Lu XF, Wen YH, *et al*. Construction of interesting organic supramolecular structures with synthons cooperation in the cocrystals of 1H-benzotriazole and hydroxybenzoic acids, Sci China Chem, 2012, 55: 2515-2522.

[14]. Bushuev M B, Virovets A V, Garcia Y, Gieck C, Sheludyakova L A, Ikorskii V N, Tremel W, Gütlich P, Mononuclear coordination compounds based on a novel chelating triazole ligand: 1-vinyl-3-acetylamino-1, 2, 4-triazole, Polyhedron, 2002, 21, 797.

[15]. Akhilesh Kumar Verma, Benzotriazole and Its Derivatives as Ligands in Coupling Reaction, *Advance in Heterocyclic Chemistry*, 2012, 101-132

[16]. Brian S. Furniss, Antony J. Hannaford, Peter W. G. Smith & Austin R. Tatchell, Vogel's textbook of practical Organic chemistry, 5th edition, 1989, 1163

[17]. Hitesh G. Raval, Sunil L. Baldania and Dimal A. Shah, Practical inorganic chemistry, Nirav & Roopal Prakashan, First Edition, 2008, 303

[18]. Purohit M.K., Srivastava S.K. Benzotriazole derivatives as antimicrobial agents, *IJPS,* 1992, 54(1), 25-27.

[19]. Upadhaya R.K., Srivastav S.D. Derivatives of *1*-(N-heteroaryl/ diphenyl aminoacetyl/propionyl) benzotriazole, *Indian J Pharm Sci.,* 1995; 57(1): 12.

[20]. Rajput A. P. and Rajput S. S. Synthesis of benzaldehyde substituted phenyl carbonyl hydrazones and their formylation using Vilsmeier-Haack reaction. *International Journal of PharmTech Research*. 2009; 1: 1605-1611.

[21]. Sanna P., Antonio C., Mohammad E., Synthesis and antitubercular activity of 3-aryl substituted-2-(1H(2H) benzotriazol-1(2) yl)acrylonitriles, Eur. J. Med. Chem; 2000,35:535−543.

[22]. Gold HS, Moellering RC Jr. Antimicrobial-drug resistance. *N Engl J Med* 1996; 335:1445-53.

[23]. Papakonstantinou-Garoufalias S, Pouli N, Marakos P, Chytyroglou-Ladas A. Synthesis antimicrobial and antifungal activity of some new 3-substituted derivatives of 4-(2,4-dichlorophenyl)-5-adamantyl)-1*H*-1,2,4-triazole. *Farmaco* 2002; 57:973-77.

[24]. Collin X, Sauleau A, Coulon J. 1,2,4-Triazolo mercapto and aminonitriles as potent antifungal agents. *Bioorg Med Chem Lett* 2003; 13:2601-05.

[25]. Purohit M.K., Srivastava S.K. Benzotriazole derivatives as antimicrobial agents, *IJPS*, 1992; 54(1): 25-27.

[26]. Upadhaya R.K., Srivastav S.D. Derivatives of *1*-(N-heteroyl/ diphenyl aminoacetyl/propionyl) benzotriazole, *Indian J Pharm Sci.,* 1995; 57(1): 12.

[27]. Ackerman P., Max S., Microbicidal Benzotriazole compounds, US Patent No: 5,322,853, 1994.

[28]. Taha M.A Eldebss, Recent Advances on the Synthesis of Pyrazole-Containing Compounds of Potent Biological Activities and Study Their Chemical Applications, *Asian Journal of Biochemical and Pharmaceutical Research*, 2014: 3(4): 356-384.

[29]. Fatima A.O., Rafat M.M., Adel A.E.K. Synthesis and biological effects of new derivatives of benzotriazole as antimicrobial and antifungal agents, *J Heterocyclic Chem*., 2002; 39; 877.

[30]. Kuo-Long Yu *et al* Fundamental Structure–Activity Relationships Associated with a New Structural Class of Respiratory Syncytial Virus Inhibitor. *Bioorg Med Chem Lett*, 13: 2141-44.

[31]. Katarzyna K. *et al*. Corrigendum to Synthesis and activity of 1H-benzimidazole and 1H-benzotriazole derivatives as inhibitors of *Acanthamoeba castellanii*. *Bioorg Med Chem*., 2004: 12: 2617.

[32]. Jagattaran D. *et al*. Effects of positional and geometrical isomerism on the biological activity of some novel oxazolidinones. *Bioorg Med Chem Lett*., 2005; 15: 337.

[33]. Prasad PD, Prathap SN, Vijaykumar JP, Sanjay J, Sudershan KA, Neelima S., Synthesis and antibacterial activity of novel (un) substituted benzotriazolyl oxazolidinone derivatives. *Bioorg Med Chem Lett*; 2005: 15: 3002–3005.

[34]. Maria Bretner *et al*, Synthesis and biological activity of 1H-benzotriazole and 1H-benzimidazole analogues – inhibitors of the NTPase/helicase of HCV and of some related Flaviviridae. *Antiviral Chem Chemotherapy*; 2005, 16: 315–26.

[35]. Asati KC, Srivastav SK, Srivastav SD. Synthesis of some new 5-arylidene-2-aryl-3-(benzotriazoloacetamidyl)-1, 3-thiozolodine-4-ones as analgesic and antimicrobial agents. *Indian J Chem.* 2006, 45B; 526-31.

[36]. Nanjunda S *et al*. Microwave-assisted synthesis of N-alkylated benzotriazole derivatives: Antimicrobial studies. *Bioorg Med Chem Lett*; 2006, 16:999–1004.

[37]. Chung-Yi Wu *et al*, Stable Benzotriazole Esters as Mechanism-Based Inactivators of the Severe Acute Respiratory Syndrome 3CL Protease. *Chem Biol*; 2006; 13: 261–68.

[38]. Prasad PD, Vijaykumar JP, Prathap SN, Sanjay J, Neelima S, Sudershan KA., Synthesis of 1-[3-(4-benzotriazol-1/2-yl-3-fluorophenyl)- 2-oxo-oxazolidin-5-ylmethyl]-3- substituted thiourea derivatives as antituberculosis agents. *Repository*; 2006; 41: 423–28.

[39]. Shukla DK, Srivastav SD., Synthesis of some new 5-[2-{(1,2,3-benztriazole)-1-yl methyl}-1′-(4′-substituted aryl-3′-chloro-2′-oxo azetidine)]-amino-1,3,4thiadiazoles: Antifungal and Antibacterial agents. *Indian J Chem*; 2008, 47(B): 463-69.

[40]. Koen HG *et al* A Structural View of the Inactivation of the SARS Coronavirus Main Proteinase by Benzotriazole Esters. *Chem Biol*; 2008, 15:597–606.

[41]. Namdeo KP., Singh VK., Prajapati SK. Synthesis of Some 2-(Substituted)-5-[(N Benzotriazolomethyl)-1, 3,4-Thiadiazolyl]-4-Thiazolidinones for their Anti-Fungal Activity. *Indian J Pharm Educ Res* 2009; 43(3): 266-71.

[42]. Rezaei Z, Khabnadideh S, Pakshir K, Hossaini Z, Amiri F, Assadpour E. Design, synthesis, and antifungal activity of triazole and benzotriazole derivatives. *Eur J Med Chem* 2009; 44:3064-67.

[43]. Wan J, Lv PC, Tian NN, Zhu HL. Facile synthesis of novel benzotriazole derivatives and their antibacterial activities. *Journal of chemical sciences.* 2010 Jul 1; 122(4): 597-606.

[44]. Singh V. K. *et al*, Benzotriazole: A Heterocyclic Molecule With Diversified Pharmacological Activities, *IJPSR*, 2017; 8(2): 446-456.

[45]. Patel P. D., Patel M. R., Kocsis B., Kocsis E., Graham S. M., Warren A. R., Nicholson S. M., Billack B., Fronczek F. R., and Talele T. T: Design, synthesis and determination of antifungal activity of 5(6) substituted benzotriazoles. *European Journal of Medicinal Chemistry* 2010; 45: 2214-2222.

[46]. Ramachandran R., Rani M., Senthan S., Jeong Y. T., and Kabilan S: Synthesis, spectral, crystal structure and in vitro antimicrobial evaluation of imidazole / benzotriazole substituted piperidin-4-one derivatives. *European Journal of Medicinal Chemistry*, 2011; 46: 1926-1934.

[47]. Dubey A., Srivastava S. K., and Srivastava S. D: Conventional and microwave assisted synthesis of 2-oxo-4-substituted aryl-azetidine derivatives. *Bioorganic Medicinal Chemistry Letters* 2011; 21: 569-573.

[48]. Carta A., Briguglio I., Piras S., Boatto G., Colla P. L., Loddo R., Tolomeo M., Grimaudo S., Cristina A. D., Pipitone R. M., Laurini E., Paneni M. S., Posocco P., Fermeglia M., and Pricl S: 3-Aryl-2-[1H-benzotriazole-1-yl] acrylonitriles-A novel class of protein tubulin inhibitors. *European journal of medicinal chemistry* 2011; 46: 4151-4167.

[49]. Gaikwad ND, Patil SV, Bobade VD. Synthesis and biological evaluation of some novel thiazole substituted benzotriazole derivatives. *Bioorganic & medicinal chemistry letters.* 2012 May 15; 22(10): 3449-54.

[50]. 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.

[51]. Patel J.S., Garg C.S. & Sen D.J. Synthesis of Novel N-Substituted 2-(1H-Benzotriazol-1-yl)-Acetohydrazide Derivatives as Antimicrobial agents. *Int J Drug Developmen Res.,* 2012; 4(2):322.

[52]. Suma BV, Natesh NN, Madhavan V. Benzotriazole in medicinal chemistry: an overview. *J Chem Pharm Res* 2011; 3: 375-381.

[53]. Sudhir M. S, Nadh R. V., and Radhika S. Antifungal activities of novel 1,2,3 – benzotriazole derivatives synthesized by ultrasonic and solvent free conditions. *Drug invention today* 2013; 5: 126 -132.

[54]. Singh V. K, Rishishwar P, and Bhardwaj P: New chemical entities (NCE's): Concept, Synthesis and Identification. *Journal of Biomedical and therapeutic sciences* 2014; 1: 85.

[55]. Jamkhandi C. M., Kumbhar P. S., Disouza J. I., and Patil S. M: QSAR study and evaluation of in vitro anti-inflammatory activity for 1h-benzotriazol-1-yl{2-hydroxy-5-[(e) phenyldiazenyl]phenyl} methanone. *European Journal of Pharmaceutical and Medical Research* 2015; 2: 1004-1010.

[56]. Farkas R, Lhiaubet-Vallet V, Corbera J, Törincsi M, Gorchs O, Trullas C, Jiménez O, Miranda MA, Novak L. Synthesis of new 2-(2-hydroxyaryl) benzotriazoles and evaluation of their photochemical behavior as potential UV-filters. *Molecules*. 2010 Sep; 15(9): 6205-16.